OFFICE OF RESEARCH ON WOMEN'S HEALTH

National Institutes of Health

FY 2005 NIH Research Priorities for Women's Health

The mission of the Office of Research on Women's Health (ORWH) is to stimulate and encourage meritorious research on women's health, including the role of sex and gender in health and disease. ORWH collaborates with the scientific, health professional and advocacy communities to implement the recommendations from the report, *Agenda for Research on Women's Health for the 21st Century (Agenda)*.

Each year, the ORWH considers the continuing gaps in knowledge from the *Agenda* or newly emerging scientific concepts to determine specific areas of research priorities for new initiatives or increased focus. The *ad hoc* Subcommittee of the *Coordinating Committee on Research on Women's Health* (CCRWH), composed of representatives from the NIH institutes and centers, reviews the previous priorities and new opportunities for priority research for ORWH to highlight in FY 2005. The Subcommittee recommendations were reviewed and approved with minor modifications by the entire CCRWH and the members of the *NIH Advisory Committee on Research on Women's Health (ACRWH)*.

In the FY 2005 ORWH research priorities, many research opportunities are described in terms of overarching themes. The priorities signify approaches and areas in which the ORWH wishes to stimulate and encourage research on women's health and the advancement of women in biomedical research careers. Basic, translational, behavioral and clinical research in women's health, especially applied to sex/gender differences, are of particular interest. These research priorities are not an exclusive list of research areas important to women's health, therefore other innovative or significant research submissions will be considered by ORWH. For FY 2005, the following overarching themes are recommended:

I. Overarching Themes For Research On Women's Health

The following four overarching themes are important for addressing research on women's health: Lifespan, Sex/Gender Determinants, Health Disparities/Differences and Diversity and Interdisciplinary Research.

Lifespan The health of girls and women is affected by developmental, physiological, and psychological age. Women's lives are marked by a continuum from intrauterine life to the elderly years: infancy, childhood and adolescence, menarche, reproductive life, the menopausal transition, postmenopausal years, the elderly, and frail elderly. Many women's lives and health status are influenced by factors such as work inside and outside the home, care-giving such as childcare and elder care responsibilities, reproductive status, and chronic illness. Each of these may influence health, disease, treatment choices, and response to therapy. Researchers should consider these variables in designing studies related to women's health.

Sex/Gender Determinants Women are characterized by both sex and gender as highlighted in the *Agenda for Research in Women's Health for the 21st Century* and the Institute of Medicine report, entitled *Exploring the Biological Contributions to Human Health: Does Sex Matter*? In this context, the term sex refers to being male or female according to reproductive organs and

functions assigned by chromosomal complement. Sex factors that contribute to the biological differences include chromosomes, reproduction, and hormones. Gender refers to socially defined and derived expectations and roles rooted in biology and shaped by environment and experience. Gender and sex are important considerations in most areas of research, including psychological, social, and behavioral studies. Consideration of these variables is critical to the accurate interpretation and validation of research affecting women's health. Moreover, these variables determine how similar or different health or disease processes may be between women or between men and women.

Health Disparities/Differences and Diversity Women are disproportionately affected by some conditions and diseases in terms of incidence, diagnosis, course, and response to treatment. Some populations of women may be at higher risk for adverse disease outcomes because of factors such as: culture, education, access to care, quality of care, and opportunities for inclusion as research subjects in clinical trials and studies. Thus, clinical research should include, but not be limited to, population-specific characteristics such as cultural diversity, racial and ethnic minorities, immigrant status, rural or inner city residency status, effects of poverty or low socioeconomic status, sexual orientation, and physical or mental disabilities.

Interdisciplinary Research With increasing understanding of the inter-relatedness and complexity of disease, the nature of scientific investigation is shifting to a multi-disciplinary collaborative approach. Advances in women's health can be better achieved by promoting partnerships in cross-disciplinary research from basic to clinical and translational research. Collaborations among researchers in academia, private industry, and federal settings, could provide access to the latest scientific tools and technologies for women's health research.

Research integrating knowledge from disparate sources and research teams with multiple areas of scientific expertise are needed in women's health. Interdisciplinary research can facilitate the integration of basic science, clinical research and translational research, population studies, behavioral and social research, and outcomes research. An additional focus on bioengineering and biomedical informatics, genomics, proteomics, imaging, and metabolomics is increasingly relevant to research on women's health.

II. Areas of Interest in Women's Health For FY 2005

Within the research continuum, studies that encourage the adoption of research findings by physicians and the public should recognize and address the important questions that still remain concerning sex differences. Research is needed to identify the optimal methods to translate knowledge gained from basic science research into clinical research and practice in order to improve clinical outcomes in women. Studies to determine the best clinical practices in the care of women, or of men, should be emphasized in order to increase the clinical knowledge base, and the ability of women to participate in the management of their health. Through interdisciplinary collaborations, research can better contribute to the development and evaluation of effective strategies to improve the health-related quality of care and quality of life for women. Better mechanisms to translate clinical research results to healthcare providers and policy makers are needed to improve women's health. The value of conveying clinical observations to basic scientists is also important.

Basic, clinical and translational research should be considered in addressing priority areas in women's health research. Some examples may include, but are not limited to:

- Studies of chromosomal, genetic, gonadal and phenotypic sex *in vitro* or in animal models
- Etiologic mechanisms to elucidate sex differences in cellular, tissue/organ,

physiological and/or immune responses to environmental and infectious agents

- Cellular and molecular studies of the mechanism of action and effects of complementary and alternative medicines and dietary supplements in the treatment of conditions or diseases that differentially affect women
- Studies of the pathogenesis of diseases that differentially affect women, including those affecting behavior and the endocrine, musculoskeletal, autoimmune, urologic, cardiovascular, ophthalmic, and neurobiological systems
- Systemic and cellular modeling of biological pathways and systems related to women's health
- Clinical trial methodology, including ethical issues and study design specific to women, novel recruitment strategies, and novel statistical analysis methodology
- Mental health studies of the incidence, severity, and treatment of depression and other addictive, mood, cognitive, and anxiety disorders, including physical and physiological stressors;
- Studies of the effects of care-giving on the health of the care-giver and the effects of the multiple/competing societal roles of women on health
- Studies of the behavioral correlates that affect the selection and advancement of women's careers in biomedical sciences
- Studies on agents for the optimization of management of menopausal symptoms
- Studies of the role of the menstrual cycle in disease initiation, course, treatment, and response to treatment; studies of the effect of pregnancy and the post partum period on disease
- Prevalence and validation of sex differences in the diagnosis and treatment of disorders and diseases differentially affecting men and women
- Develop treatments and other interventions for specific diseases that have enhanced clinical presentation in women including, but not limited to diseases of the metabolic, endocrine, autoimmune, urologic, ophthalmic, oral, reproductive, musculoskeletal, neurological and cardiovascular systems
- Special trans-NIH research collaborations in areas such as Chronic Fatigue Syndrome and uterine fibroids

III. Special Emphasis Areas For FY 2005

For FY 2005, the ORWH is especially interested in fostering research in women's health in the high priority areas of prevention and treatment, and interaction of sex and genetics/pharmacogenomics.

Prevention and Treatment

Increased knowledge into methods to prevent conditions and diseases, or to better treat them, can result in significant improvements in the quality and length of women's lives. Prevention research spans the continuum from the most basic biological studies to understanding the basis and effects of risk behaviors across the lifespan, and the interventions to change them. Examples of needed prevention research studies in women's health include, but are not limited to:

- Research to identify and validate biomarkers of disease pathogenesis and risk and their applications to disease prevention, early detection and treatment, including the development of novel tools
- Studies of the impact of diet, nutrition, hormones, exercise, weight patterns, including obesity and eating disorders, tobacco, alcohol and drug abuse, and violence on health
- Research on reproduction, from menarche, including pregnancy to the menopausal transition, with regard to

the susceptibility to, and protection from, diseases and conditions

- Studies of the factors which are involved in disease initiation and progression in order to develop effective preventive and curative strategies
- Development, testing, and validation of preventive and curative strategies for conditions and diseases, including but not limited to: sexually transmitted diseases, cancer, coronary artery disease, stroke, obesity, musculoskeletal disorders, addictions, and chronic multi-system diseases
- Studies of the effect of biological, behavioral, cultural, social, economic, and environmental factors on susceptibility to, or protection from, disease and response to treatment

Sex and Genetics/Pharmacogenomics

While there has been much activity in the last few years in identification of the function of genes and their effect on treatment, research on the effects of sex as a modifier of gene function and response is under-investigated. The sequencing of the human genome allowed researchers to define the role of genetic polymorphisms and pharmacogenomics on development, course, and response to current treatments. However, the role of confounding factors, including sex, on the function of genes and genetic polymorphisms in disease incidence, course, and response to treatment has been largely ignored. Emphasis in this emerging area is needed particularly in those diseases that disproportionately affect women. For example, studies of:

- Determination of sex differences that may modify the role of known gene defects or polymorphisms in diseases; effect of phases of the menstrual cycle, hormones, pregnancy, and menopause on genetic penetrance of disease
- Mechanism of sex effects on gene expression
- Genetic, molecular and cellular basis of action of pharmacologic agents known to have differential effects in women and men
- Studies of the interaction of environmental exposures and genetic polymorphisms in diseases common to women; role for genes known to be differentially expressed in women in the incidence, course, and response to treatment of common diseases
- Impact of sex on genetic differences underlying pharmacokinetics, pharmacodynamics, drug efficacy and their adverse effects; development of novel methods of analysis to assist in discerning interactions of sex and genes in mechanisms of disease initiation, course, and response to treatment
- Importance of age, sex, and gene interactions in diseases affecting women; genetic polymorphisms that modify action of diet, drugs, or toxins during pregnancy on the mother and child; differences in gene expression occurring prenatally, during puberty or pregnancy and beyond