May 20, 2014

The Honorable Margaret Hamburg
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Hamburg:

We submit this letter on behalf of the 46 undersigned groups and two individual signers, representing millions of U.S. women, the providers who care for them, and the advocates who seek to promote their health and well-being.

Twenty-five years of advances in biological medicines have dramatically changed the therapeutic options available to patients and prescribers. Newer options hold even greater promise for treating and possibly curing debilitating diseases.

Women patients and their advocates have a number of reasons to take special interest in the proper use of biologic medicines. It is well-established that many diseases and conditions affect women and men differently and that the same is true of the therapies that treat them. We appreciate the steps that the Food and Drug Administration (FDA) has taken to make it more likely that medical research and treatments for diseases and conditions are analyzed to identify sex-based disparities in outcomes and side effects. This is increasingly important because:

- Sex is a key factor in the onset, prevalence, and severity of diseases and chronic conditions. These differences are significant and must be taken into consideration in treatments.
- Many of the diseases that are and will be treated through the use of biologics disproportionately affect women. Cancer is just one example where differences in race and sex can very much increase a patient's possibility of being impacted.
- Many diseases place a heavier burden on women than on men (for example, heart disease, cancer, rheumatoid arthritis and osteoporosis); however, treatment guidelines are based largely on data on men. Women also rely more on medical systems than men do and are likely to seek treatment sooner.[i]
- Autoimmune diseases are one of the top 10 leading causes of death among U.S. women aged 65 and under. Many autoimmune diseases are treated by biologics and some, such as lupus and Sjögren's Syndrome, strike women nine times more often than men.[ii]
- Sex-based differences are observed in response to many drugs. Females have a 1.5 to 1.7 fold greater risk of developing an adverse drug reaction, and several drugs have been withdrawn from the market over the last two decades for sex-based adverse events.[iii]

Further, because women are often underrepresented in clinical trials, little may be known about impacts of treatments on female populations until after FDA approval when a new biologic is first used in a heterogeneous population through clinical care. This is compounded by the historic and continuing lack of understanding of sex-based differences in clinical trials. Specifically:

- The number of women participating in clinical trials has increased during the last two decades, but women are still underrepresented in clinical trials in general. Some of the overall increase can

be attributed to the greater number of women-only trials (of therapies for diseases that affect only women). Even when women are included in clinical trials, the results are often not analyzed separately by sex.[iv]

- A recent Institute of Medicine consensus report found that "limitations in the design, analysis, and scientific reporting of health research have slowed progress in women's health."[v]

This means that for millions of female patients, any potential increase or decrease in effectiveness of a biologic, along with side effects and adverse reactions, will only be discovered after the treatment is approved and under active use. Thus, the complexity and variability of treatment paradigms using biologics will be a continuing concern to providers serving female patients.

As states across the country look to the FDA for guidance on issues surrounding biosimilarity, interchangeability, and therapeutic substitution, the agency's views on sex and genomic-based differences will be crucial.

For all these reasons, as FDA moves forward to approve biosimilars, we believe it is imperative that all biologics have distinguishable names. Distinguishable names will enable the gathering of sufficient data to ultimately allow providers to fully understand how all biologics – including biosimilars – are performing for both men and women. Furthermore, as the FDA continues to address patient safety, we urge states to ensure the safety of women, and all patients, by enacting legislation that mandates physician notification and record keeping when biosimilars are substituted. This will lessen the inevitable confusion and assure optimal medical care in the use of biosimilars among female populations.

We urge the FDA to give serious consideration to the voices specifically focused on and attuned to sex-based disparities in health as it arrives at a policy for naming biosimilars. We thank you for the opportunity to raise our voice on behalf of female patients, and the caregivers and providers they trust.

Sincerely,

Society for Women's Health Research

Academy of Women's Health

American Autoimmune Related Diseases Association

American Behcet's Disease Association

Barbra Streisand Women's Heart Center at Cedars-Sinai Heart Institute

Black Women's Health Imperative

Center for the Study of Sex Differences in Health, Aging and Disease at Georgetown University

Coalition for Pulmonary Fibrosis

Colon Cancer Alliance

Crohn's & Colitis Foundation of America

Digestive Disease National Coalition

Foundation for Women's Health

Global Healthy Living Foundation

HealthyWomen.org

International Cancer Advocacy Network

International Pemphigus & Pemphigoid Foundation

International Society for Gender Medicine

Interstitial Cystitis Association

Jewish Women International

Kidney Cancer Association

Lupus Alliance of Long Island/Queens

Lupus Alliance of Upstate New York

Lung Cancer Alliance

Lupus Foundation of America

Lupus Foundation of Colorado

Lupus Foundation of Florida, Inc.

Lupus Foundation of Mid and Northern New York, Inc.

Lupus Foundation of Southern California

Michigan Lupus Foundation

National Adrenal Diseases Foundation

National Fibromyalgia & Chronic Pain Association

National Organization of Women

New York State Rare Disease Alliance

Pulmonary Hypertension Association

RESOLVE: The National Infertility Association

Scleroderma Foundation

Sex and Gender Women's Health Collaborative

Sjögren's Syndrome Foundation

The Endometriosis Association

The Endometriosis Foundation of America

The Marfan Foundation

U.S. Pain Foundation

Vasculitis Foundation

Virginia Commonwealth University Institute for Women's Health

WomenHeart: The National Coalition for Women with Heart Disease

Women's Health Research Institute at Northwestern University

Marek Glezerman, MD, President
International Society for Gender Medicine

Theresa Rohr-Kirchgraber, MD, FACP, Executive Director
Indiana University National Center of Excellence in Women's Health

cc: Marsha Henderson, MCRP, Assistant Commissioner for Women's Health, FDA

[Members of the Congressional Caucus for Women's Issues]

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[i] http://www.nap.edu/openbook.php?record_id=13307&page=6
[ii] http://www.aarda.org/autoimmune-information/autoimmune-disease-in-women/
[iii] http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/WomensHealthResearch/UCM334959.pdf
[iv] http://www.nap.edu/catalog.php?record_id=13307
[v] http://www.nap.edu/openbook.php?record_id=13307&page=3