November 1, 2012
The Honorable Margaret A. Hamburg, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993


Dear Commissioner Hamburg:

On behalf of the American Association of Clinical Endocrinologists, thank you for the opportunity to provide the following comments regarding the Prescription Drug User Fee Act’s Patient-Focused Drug Development Initiative.

The American Association of Clinical Endocrinologists (AACE) represents over 6,000 endocrinologists in the United States and abroad. AACE is the largest association of clinical endocrinologists in the world. The majority of AACE members are certified in Endocrinology and Metabolism and concentrate on the treatment of patients with endocrine and metabolic disorders including diabetes, thyroid disorders, osteoporosis, growth hormone deficiency, cholesterol disorders, hypertension and obesity. AACE members are committed to providing the highest quality of care to the patients they serve.

AACE supports the mandate of the FDA Safety and Innovation Act that the FDA consider perspectives from patients with life-threatening diseases in evaluating new drug approvals. It is appropriate that this information be incorporated into the overall risk/benefit formulation in adjudicating new drugs in a patient-focused drug development format. As advocates for the care of patients with endocrinologic and metabolic diseases, AACE believes that it is highly appropriate that obesity, diabetic ulcers, diabetic foot infections, peripheral neuropathy and female sexual dysfunction be nominated for diseases deserving of public meetings and patient-focused input. We also suggest that osteoporosis be added to the list, potentially as a replacement for fracture healing.

Obesity:

Obesity is a complex, multifactorial condition characterized by excess body fat. It must be viewed as a chronic disorder that essentially requires perpetual care, support, and follow-up. AACE enthusiastically supports the inclusion of Obesity in the patient-focused drug development initiative. As a chronic disabling metabolic disease, obesity is responsible for a heavy burden of patient suffering and social costs. In the United States, over 100 million adults are obese and their obesity is responsible for nearly $150 billion per year in direct (medical expenses) and indirect (value of lost productivity) costs.
Earlier this year, patient perspectives were appropriately considered in understanding the severity of the disease in relationship to the adequacy of existing therapeutic options. The result was the first obesity drug approvals in more than a decade. This has provided health care providers with new tools for treating obesity according to the medical model as we apply evidence-based interventions to reduce morbidity and mortality in our patients. The FDA should continue this strategy to develop new treatments for obesity.

Peripheral Neuropathy, Diabetic Foot Infections and Diabetic Foot Ulcers:

It is important when considering drug approval for conditions such as painful diabetic neuropathy, diabetic foot ulcer and diabetic foot infections, that consideration of the debilitating nature of the disease and not just the potential side effects of potential therapies, are considered. Traditional measures of disease severity (mortality, complications, etc.) may not fully encompass the entire patient experience with the disease. For example, many patients with diabetic foot ulcers are forced to curtail their activities for years until the ulcers heal. This disruption of the patient's ability to experience life to its fullest should be considered when evaluating the potential benefit of new therapies for diabetic foot ulcers. It is important for regulators to understand the importance to the patients of these conditions.

Painful diabetic peripheral neuropathy is a condition that affects 24.9% of patients with type 2 diabetes. At the present time 3 drugs are approved for treating pain associated with this condition and no drugs have been approved that alter the disease course. Analgesia in painful neuropathy is difficult and challenging. Opiates are largely ineffective and habituating in the end. Research on pain modifying agents as well as those agents which may alter pain awareness is mandatory. Further, although finding drugs to treat painful neuropathy is important, finding therapy to alter the course of diabetic neuropathy is also very important. In the end, prevention of neuropathy by improved methods of glycemic control may be our most effective strategy for the treatment and prevention of this serious complication of diabetes mellitus.

Early detection of neuropathy is mandatory if the pathogenesis of the disease is to be interrupted. An end stage patient with diabetic neuropathy presents with numbness which poses multiple problems. Since numbness and lack of sensation is the end stage of the process, patients often interpret a reduction in pain and burning as evidence of improvement rather than the more ominous progression of disease. When numbness occurs in the feet, and if the patient has poor circulation, the patient is at great risk for ulceration of the foot. Ulceration of the foot often leads to difficulty healing, foot infection and gangrene. This progression of disease often leads to amputation. Indeed, diabetes is the number one cause of lower extremity amputation in the United States.

Treatments for painful neuropathy are extraordinarily important to improve quality of life for our patients. Treatments that alter the course of neuropathy (preserve sensation) should help prevent foot ulcerations and infections and decrease the frequency of lower
extremity amputation. Having a patient with these conditions testify about his/her experience with the present therapies and how these conditions affect him/her would be very beneficial for regulators to increase the benefit side of the risk benefit equation. AACE feels that having patients testify would be beneficial as long as carefully conducted studies addressing the risks and benefits are still the major focus of the decisions made by the FDA.

Female Sexual Dysfunction:

The National Health and Social Life Survey documented that approximately 25 to 30% of women experience sexual dysfunction including lack of interest in sex, inability to achieve orgasm, and lack of pleasurable sex. Approximately 85% of women with sexual dysfunction are diagnosed with hypoactive sexual desire disorder. Approximately 30% of menopausal women in United States have low sexual desire. The causes of low sexual desire in women are complex, including general health issues, psychiatric disorders, and marital problems.

The treatment of female sexual dysfunction is directed primarily to correcting health and psychiatric disorders and marital counseling. The relative contributions of androgens and estrogen to female sexual functioning is controversial. There is no clear association between androgen levels and female sexual function. However, clinical trials in postmenopausal women with sexual dysfunction and adequate estrogen therapy have demonstrated a benefit of transdermal testosterone.

There is a clear need for more effective treatment options for female sexual dysfunction, especially in postmenopausal women.

Osteoporosis:

Osteoporosis is a silent disease that often goes undetected until a fall or other injury results in a broken bone. Not only are these fractures painful, they can be deadly or devastating in terms of quality of life: six months after a hip fracture only one in four people walk independently and one out of every four who lived independently requires nursing home care for a least one year after their hip fracture.

Osteoporosis is pervasive among older women. Seventy-three percent (73%) of women over the age of 65 have osteoporosis or low bone mass, a condition which marks the beginning of the disease. Fractures from osteoporosis are more common in older America women than heart attack, stroke, and breast cancer combined. More women in this country die each year from complications of hip fracture than from breast cancer.

The best defense against osteoporosis is early diagnosis using the dual energy x-ray absorptiometry test (DXA) followed by appropriate treatment. A recent study of women age 65 and over in the Medicare fee-for-service program found that those who had a
DXA had 35% fewer hip fractures in the following three years than those who did not. Despite the availability of effective therapeutic agents, osteoporosis is not only underdiagnosed but also undertreated. According to Medicare's HEDIS criteria, only about 1 in 5 women with a fracture is either tested or treated. Concerns about the safety of treatments, often misunderstood, prevent patients and providers from initiating therapy or to stop treatment unnecessarily. New agents are under development but better understanding of the state-of-the-art would be beneficial.

Once again, we thank you for the opportunity to comment on the patient-focused drug development initiative and for your consideration of these views. If AACE can provide any assistance, please do not hesitate to contact Mr. Michael Williams, Healthcare Regulatory Policy Project Coordinator, at mwilliams@aace.com.

Sincerely,

Alan J. Garber, MD, PhD, FACE
President

George Grunberger, MD, FACP, FACE
Chair, AACE FDA Issues Committee