

November 7, 2005

0784 5 NOV -8



GlaxoSmithKline

Management Dockets, N/A
Dockets Management Branch
Food and Drug Administration
HFA-305
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

GlaxoSmithKline
PO Box 13398
Five Moore Drive
Research Triangle Park
North Carolina 27709-3398
Tel 919 483 2100
www.gsk.com

Re: NAS 0; Not Product Specific

**General Correspondence: Comments on "Critical Path Initiative;
Developing Prevention Therapies; Planning of Workshop" [Docket No. 2005N-0355]**

Dear Sir or Madame:

Reference is made to the notice published by the FDA in the Federal Register on August 3, 2005, to invite written comments on the proposed scope of a workshop to explore approaches and potential obstacles to developing drugs, disease biomarkers, medical devices and vaccines to prevent or reduce the risk of illness, as part of the Agency's Critical Path Initiative. The purpose of this letter is to provide comments on scope of this workshop, "Critical Path Initiative – Developing Prevention Therapies."

GlaxoSmithKline is a research-based pharmaceutical and biotechnology company. Our company is dedicated to the discovery, development, manufacture, and distribution of medicines and vaccines that enable people to lead longer, happier, healthier, and more productive lives. GSK has a long history of productive research and development of products to treat diabetes, and in view of our longstanding work in this field and our substantial interest in the topic, we welcome this opportunity to provide comments for FDA's consideration.

Type 2 diabetes mellitus (T2DM) affects approximately 150 million people worldwide and is projected to increase to 225 million by 2010. It is a disease associated with significant risk of microvascular and macrovascular complications, and accounts for 2.5% to 15% of annual healthcare expenditure globally. The presence of dysglycemia even at levels below that defined as diabetic, i.e. impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), places individuals at increased risk of cardiovascular (CV) events and for progression to overt diabetes and its associated sequelae.

Delaying or preventing the onset of T2DM in a group at high risk for developing the disease should be considered a benefit in terms of morbidity and mortality. Data from

2004N-0355

C19

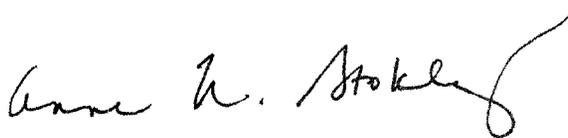
both the UK Prospective Diabetes Study (UKPDS) and Diabetes Control and Complications Trial (DCCT) suggest that blood glucose levels should be maintained as close to normal as possible in order to reduce microvascular and macrovascular complications. It is well established that abnormalities in glucose metabolism, i.e., impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), emerge prior to the development of T2DM and can be considered intermediate stages in the diabetes disease process. There is also accumulating evidence that microvascular disease exists prior to the diagnosis of T2DM, and IGT has long been identified in epidemiological studies as a risk factor for CV disease and mortality.

Individuals with IGT and/or IFG may already be receiving health care services for co-morbid conditions such as obesity, dyslipidemia or hypertension; thus, there is an opportunity for intervention to prevent progression to overt T2DM. While the efficacy of intensive lifestyle intervention (i.e., sustained weight loss and exercise) in the prevention of T2DM was shown in both the Finnish Diabetes Prevention Study and the US Diabetes Prevention Study, successful implementation of these intensive lifestyle modifications outside the auspices of a controlled clinical trial may not be attainable. Weight re-gain or worsening glucose tolerance are common problems which occur when lifestyle intervention alone is used to prevent T2DM and its co-morbid conditions.

The benefits of delaying or preventing progression to T2DM in individuals with IGT and/or IFG may be considerable. The American Diabetes Association, the American College of Endocrinology and the American Association of Clinical Endocrinologists recommend screening patients at risk of developing T2DM. Once these individuals are identified, however, the question remains as to what treatment options should be made available. GSK believes patients and prescribers should be appropriately informed on the risk: benefit of suitable pharmaceutical therapies in prevention of Type 2 diabetes.

We appreciate this opportunity to provide input for agenda topics for the workshop. This submission is provided in triplicate. Please contact me at (919) 483-6405 if you require clarification or have any questions about these comments. Thank you.

Sincerely,



Anne N. Stokley, M.S.P.H.
Director, Policy, Intelligence & Education
US Regulatory Affairs