June 1, 2004

U.S. Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket 2004Q-0144 Health Claim Petition,
Chromium Picolinate

Dear Sir or Madame:

I submit this letter in support of the qualified health claims for chromium picolinate as a dietary supplement to: [i] reduce the risk of insulin resistance; [ii] reduce the risk of abnormally elevated blood sugar levels; and [iii] reduce the risk of type 2 diabetes. Appropriate health claim statements to these effects are warranted by evidence derived from experimental studies and, most importantly, from randomized clinical trials (RCT) as well as the impact on public health of the rapidly growing prevalence of type 2 diabetes in the U.S.

The risk for type 2 diabetes and its microvascular sequela can be reduced by changes in diet, including increases in chromium III intake (in particular, chromium picolinate) and physical activity targeted to improved nutritional status and ideal body weight and composition. Chromium picolinate as a dietary supplement represents a useful tool for reducing the risks associated with impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes.

Meta-analyses of the effect of chromium supplementation in people with prediabetes and type 2 diabetes have provided mixed results due to inadequate consideration of the dose and form of chromium. Chromium picolinate is the most bioavailable form of nutritional chromium. This factor appears to account for the high rate of improvement in clinical outcomes in protocols employing chromium picolinate. For example, the following RCT utilizing 200-1000 μg/d chromium and found significant reductions in fasting glucose, glycated hemoglobin (HbA1c), and other biomarkers of improved glucose control or insulin status among individuals with type 2 diabetes or gestational diabetes: Ghosh et al. (*J Nutr Biochem* 2002;13:690-7); Jovanovic-Peterson et al. *J Trace Elem Med Biol* 1999;12:91-7); Anderson et al. *Diabetes* 1997;46:1786-91); and Evans (*Int J Biosocial Med Res* 1989;11:163-80). Further, preliminary results from two recent RCT are consistent with these reports (Feng et al. *Diabetes* 2002:51:A469; Houweling et al. *Diabetologia* 2003;46:A261) as is an RCT conducted in obese prediabetics with mild fasting hyperinsulinemia but without hyperglycemia (Cefalu et al.

J Nutr 2002;132:1107-14). These well-controlled RCT have examined a total of 478 subjects. These results are in contrast only with the RCT by Lee & Reasner (*Diabetes Care* 1994;17:1449-52) who found no effect of 200 µg chromium picolinate (the lowest dose tested in clinical trials) on fasting glucose and HbA1c in 30 type 2 diabetics also receiving drug therapies.

It is important to note that additional clinical trials, but conducted with an "open label" design, involving 1099 patients with type 1 or 2 diabetes, have also demonstrated beneficial outcomes on glucose homeostasis. It is worth noting as well that chromium picolinate is effective in reducing elevated plasma glucose but has no effect in individuals with normal plasma glucose or glucose tolerance. Thus, chromium picolinate supplementation at 200-1000 µg/d is effective in reducing risks associated with insulin resistance, prediabetes, and type 2 diabetes. This efficacy suggests as well the ability chromium picolinate to delay the risk of progression from prediabetes to diabetes and to reduce the risk for diabetic sequale, including microvascular diseases (retinopathy, nephropathy, and neuropathy) and cardiovascular disease.

In the context of a qualified health claim for chromium picolinate, it is worth noting that the Institute of Medicine (IOM) currently suggests a daily Adequate Intake (AI) for chromium of 35 µg and 25 µg for men and women aged 19-50 years, respectively. In contrast, the Daily Value (DV) set by the FDA in 1997 for chromium is 120 µg. Accurate measures of dietary intakes of chromium are not available from current databases, but various reports suggest a range of daily intakes among Americans between <20-54 µg. Although the AI is reduced by 5 µg for people over 50 years, some data indicates an age-related decrease in chromium status and suggests an increased requirement for chromium in older adults to reduce their increased incidence of impaired glucose tolerance and risk for chromium depletion. Importantly, chromium picolinate is very safe (recognized as GRAS and lacking a Tolerable Upper Level [UL]), with an estimated potential toxicity occurring at 70,000 µg/d (Mertz. *Nutr Rev* 1995;53:179-85).

In conclusion, I feel that qualified health claims for chromium picolinate as a dietary supplement to reduce the risk of insulin resistance, abnormally elevated blood sugar levels, and the risk of type 2 diabetes is substantiated by the totality of available scientific evidence and may assist Americans in better helping themselves promote their health.

Sincerely,

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