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Linda Kahl
Division of Product Policy
Mail Code HFS-205
FDA
200 "C" St, SW
Washington, DC 20204

Dear Dr. Kahl,

We are writing in reference to the application for GRAS status for isoflavones, such as genistein, by ADM. We oppose GRAS status because there is abundant evidence that some of the isoflavones, including genistein and equol, are toxicants. This is true for a number of species, including humans. Additionally, the adverse effects in humans occur in several tissues and, apparently, by several mechanisms.

Genistein is clearly estrogenic; it possesses the chemical structural features necessary for estrogenic activity (Miksicek, 1998, Sheehan and Medlock, 1995, Tong, et al, 1997) and induces estrogenic responses in developing and adult animals and in adult humans. In rodents, equol is estrogenic and acts as an estrogenic endocrine disruptor during development (Medlock, et al, 1995a,b). Faber and Hughes (1993) showed alterations in LH regulation following developmental treatment with genistein. Thus, consumption of isoflavones during pregnancy in humans could be a risk factor for abnormal brain and reproductive tract development.

Additionally, isoflavones are inhibitors of the thyroid peroxidase which makes T3 and T4. Inhibition can be expected to generate thyroid abnormalities, including goiter and autoimmune thyroiditis. There exists a significant body of animal data that demonstrates goitrogenic and even carcinogenic effects of soy products (cf., Kimura et al., 1976). Moreover, there are significant reports of goitrogenic effects from soy