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COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

WORKING GROUP ON PHYTOESTROGENS

Submission from Dr Doerge & Dr Sheehan (received 04/08/00)

Background

1. Dr Doerge & Dr Sheehan are scientists at the US National Centre for Toxicological Research. They are opposed to the FDA's authorisation for health claims on food containing soya protein. They have written a letter of protest to the FDA entitled "Food labelling: health claims; soy protein and coronary heart disease". This letter was published on the ABC News website.

Submission

2. Dr Doerge and Dr Sheehan identify the soya isoflavones, genistein & daidzein & its metabolite, equol, as estrogens. They propose that genistein & equol disrupt development in animals & thus could be a risk factor for abnormal human brain & reproductive tract development. They point to studies in rhesus monkeys (Harrison *et al*, 1998) where estradiol levels increased (50-100%) in genistein fed animals & that estradiol is a risk factor in breast cancer. In addition, increases in estradiol were reported in monkey foetuses (70%) & that this stage of development is sensitive to exposure to estrogens as highlighted by diethylstilbestrol (DES) induced malformations & malignancies in humans.

3. The authors comment that although there are potency differences between DES and phytoestrogens, they consider that no dose is without risk as a study showed that a threshold level could not be established for 31 hormone-mimicking chemicals (Sheehan, 1998a). The authors recommend that transplacental passage of isoflavones should be considered in light of the adverse effects observed with the synthetic estrogen compound DES.

4. The authors identify a study of the goitrogenic & carcinogenic (Kimura *et al*, 1997) effects of phytoestrogens on the thyroid gland & a study reporting the higher incidence of autoimmune thyroiditis in children fed soy infant formula compared to other forms of milk (Fort *et al*, 1986 & 1990). Dr Doerge & Dr Sheehan conclude that isoflavones are goitrogenic (Divi RL *et al*. 1997; Kimura S *et al*. 1976; McCarrison R. 1933; Fort *et al*. 1986).

5. Potential associations between consumption of isoflavones and increased risk of dementia/Alzheimer's disease & brain atrophy are discussed (White *et al*, 1996a & 1996b) & the authors conclude that as estrogens are necessary for brain function & isoflavones inhibit aromatase enzymes (Irvine *et al*, 1998) there is a mechanistic basis for these effects. The Working Group considered the earlier study by White *et al* (1996a) at the January 2001

meeting. The later study by White L *et al*, (1996b), on the incidence of dementia in Japanese-American men in Hawaii, was not considered by the Working Group. However, it does not make any associations between phytoestrogen intake & dementia.

6. The authors conclude that given the difficulty in detecting toxicities with long latencies they are unconvinced that the long history of apparent safe use of soya products can provide confidence that they are without risk. They point out that whilst the FDA regulates estrogenic & goitrogenic drugs, no similar safe guards are in place for foods.