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

WORKING GROUP ON PHYTOESTROGENS

Submission from Dr Mike Fitzpatrick (received 12/07/00)

Background

1. In conjunction with Mr Richard James (see submissions PEG/2001/4, PEG/2001/7 & PEG/2001/13), Dr Fitzpatrick runs the Soy Online Service website from New Zealand. The website aims to raise awareness on potential health effects of soy and soya-based products. Dr Fitzpatrick is a consultant toxicologist & is concerned about the toxicity of soya-based products & has submitted the following articles for consideration by the Working Group.

FOOD COMMISSION BRIEFING PAPER (1998)

2. The paper, written with Sue Dibb, outlines health concerns arising from the use of soya-based infant formula and states that infants fed soya formulae have plasma isoflavone levels comparable to those that produce estrogenic effects in animals & menstrual cycle disruption in pre-menopausal women. A number of studies are highlighted. All have been included in papers presented to the Working group with the exception of:

- Study on soya bean induced goiter in infants Ripp (1961). Many studies of the interaction of soya foods with the thyroid gland were presented in the Position Statement on Soya Based Foods & the Thyroid Gland (Dr Hindmarsh) at the January 2001 meeting.
- A study by Freni-Titulaer *et al* (1986) indicating that a significant positive correlation between soya formulae & premature thelarche in Puerto Rico.
- Studies on the ability of phytoestrogens to modulate of steroid hormone synthesis & metabolism were presented to the Working Group at the June 2000 meeting (PEG/2000/10) with the exception of Keung (1995). However, this study examines the effects of isoflavones on bacterial enzymes.
- The paper notes that phytoestrogens are endocrine disrupters (Pope *et al*, 1954) & reproductive & developmental toxicity has been observed in a number of animal species such as cheetah (Setchell *et al*, 1987), quail (Leopald, 1976), mice (Drane *et a*l, 1980; Carter *et al*, 1955; Matrone *et al*, 1956), rats (Kimura *et al*, 1976), sturgeon (Pelissero et al, 1991) & sheep (Braden *et al*, 1967). Many of these studies include observations in wildlife & therefore have not been conducted under controlled experimental conditions.

4. The paper discusses the UK Food Advisory Committee (FAC) request (1996) that manufacturers of soya formulae investigate means of reducing the isoflavone content. It is suggested that isoflavone levels could be reduced by ethanol extraction. However, manufacturers appear reluctant to reduce the

isoflavone content. It is pointed out that low-phytoestrogen formulae has been developed but the Infant & Dietetic Association (IDFA) (see submission PEG/2001/9) claim additional processing to reduce levels of isoflavones would affect the nutritional quality of the formula.

5. The paper concludes that it is irresponsible of soya formulae manufacturers to place infants at risk & recommends that isoflavones be removed from soya formulae.

6. An addendum to the original paper includes reports that soya milk has never been used for feeding infants in China (Guy, 1936 and Guy et al, 1938) & therefore Asian infants may not be exposed to phytoestrogens at an early age. A study by Ishizuki *et al* (1991), also presented in the 'Position statement on Soya Foods & thyroid function' (Dr Hindmarsh), demonstrating a suppressive effect of soya protein on thyroid function is highlighted. The paper also points towards studies that suggest isoflavones in soya may have a proliferative effect on the breast. Thus, increasing the risk of breast cancer. Two *in vitro* studies demonstrating that isoflavones have a proliferative effects on MCF-7 cells (Dees *et al*, 1997; Hsieh CY *et al*, 1998) & the study presented in the adverse effects paper (PEG/2000/22) describing increases in nipple aspirate fluid of pre-menopausal women ingesting soya (Petrakis *et al*, 1996).

SOY ISOFLAVONES: A PANACEA OR POISON?

7. This article by Dr Fitzpatrick (as only part of the article was submitted the full article was obtained and summarised here) was published in Health Healing & Wisdom, a journal of the Weston A Price Foundation (see submission PEG/2001/2). The article was submitted to the FDA in an effort to prevent inclusion of isoflavones in the GRAS (Generally Recognised as Safe) list of food & medical ingredients after Dr Fitzpatrick reviewed Archer Daniels Midland (see submission PEG/2001/10) application to the FDA.

8. Dr Fitzpatrick suggests that Archer Daniels Midland's claim that isoflavones have a long & safe history cannot be substantiated as the soybean consumed in Asia (*Glycine soja*) is very different from the modern cultivar (*Glycine max*) used by industry. Dr Fitzpatrick points out that 'mass exposure' to isoflavones has only occurred in the last 30 years due to incorporation of soy protein into foodstuffs. Therefore, their safety is yet to be determined.

9. The paper suggests isoflavones are endocrine disrupters & are reproductive & immuno toxins. With the exception of a German paper, Tönz *et al*, (1997) all the original scientific literature considered by author was presented in the adverse effects paper (PEG/2000/22) or included in the Food Commission paper (see above). He recommends that extensive epidemiological studies be undertaken with clearly identified endpoints & that until the safety of isoflavones is verified by these studies it should be concluded that soy isoflavones are unsafe.

10. A study describing the mortality of young calves fed a soya milk or ethanol-extracted soya milk highlighted by Dr Fitzpatrick was not considered by the Working Group. The study reported 4/20 calves died after ingesting extracted soya milk compared to 9/20 fed unprocessed soya milk. It was suggested that 'phenolic compounds' were the likely toxins (Gardener *et al*, 1990).

11. Dr Fitzpatrick concludes that there is little evidence for beneficial effects of phytoestrogens & that GRAS status of soy isoflavones is flawed as the supporting document entitled 'An information document reviewing the safety of soy isoflavones used in specific dietary applications' contains factual errors, misrepresents cited authors and does not present the full body of evidence. Dr Fitzpatrick also recommends that the FDA denies soy isoflavones GRAS status.

SOY FORMULAS AND THE EFFECTS OF ISOFLAVONES ON THE THYROID

12. This article, written by Dr Fitzpatrick, was published in the New Zealand Medical Journal (2000). The article describes the effects of soy infant formula on the thyroid & the levels of dietary exposure to isoflavones. Many of his arguments were presented in the preceding articles.

13. The paper identifies studies of soya, which show that it is goitrogenic in humans & animals. Dr Fitzpatrick estimates an isoflavone intake of 0.33mg/kg bw/d genistein & 0.14 mg/kg bw/d daidzein after ingestion of 30g/d of soybeans, a quantity shown to be goitrogenic (Ishizuki *et al*,1991). He notes that intake of infants fed soy infant formula is 5.4 mg/kg bw/day genistein and 2.3 mg/kg bw/day daidzein (Setchell et al, 1997), greater than those levels shown to be goitrogenic. He also estimates exposure from dietary supplements (0.57 mg/kg bw/d genistein) are higher than those levels that have produced goitrogenic effects. Dr Fitzpatrick concludes that soya contains goitrogenic agents and that infants fed soya formulae & consumers of isoflavone supplements are at risk of thyroid damage. He suggests that monitoring the thyroid status of high soy consumers and users of soya-based dietary supplements is warranted.

IF YOU EAT SOY, WATCH YOU THYROID FUNCTION; NEW STUDY

12. The article is published in True Health (1997), a quarterly newsletter from Carotec Inc, a retailer of nutritional supplements. The article highlights one study (Divi et al, 1997) describing anti-thyroid activity of soya. This study was presented in the 'Position statement on soya foods & thyroid function'.