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**Norwegian Spruce Lignans Address Women's Health Issues and Heart Health**

*Directly Raising Enterolactone Levels is the Key to Benefits*

**ANAHEIM, CA – March 24, 2006 –** A new dietary supplement ingredient, HMRLignan™, from Linnea Inc. will be raising consumers' awareness and interest in their circulating enterolactone levels.

Plant lignans, typically found in whole or unprocessed foods such as flax and sesame seeds and fruits and vegetables, are now widely recognized to be beneficial to human health. Upon ingestion, lignans are converted by gut flora to the human lignan metabolite enterolactone that, like isoflavones, has a weak estrogen-like activity. Lignans are now acknowledged as a primary source of dietary phytoestrogens in both the Asian and Western diets.

However, the outcomes of changing lifestyle for American women and men has been increasingly poor diet selection and increased consumption of overly processed food, which leaves daily lignan intake below levels required to maintain the body's own production of the circulating enterolactone. Average lignan intake in the US diet is less than 1mg per day; well below the levels that research indicates to achieve health benefits.

As an alternate source of lignans, HMRLignan™ (hydroxymatairesinol) is a highly bioavailable and efficient precursor of enterolactone. HMRLignan™ is standardized to contain 80,000 mg/100 g of lignans and the daily dosage to raise enterolactone levels is 10 - 30 mg daily. Derived from Norway spruce (*Picea abies*) HMRLignan™ is a direct enterolactone precursor dietary supplement. It is a proprietary and patent protected product developed in Finland by Hormos Medical Corporation, and manufactured and marketed worldwide under license by Linnea, Switzerland.

HMRLignan™-- taken daily either as tablets and capsules or in fortified foods -- efficiently boosts circulating enterolactone, helping maintain a soft hormonal activity which may ease the symptoms of menopause and support breast health and healthy cardiovascular function.

“The key is to raise circulating enterolactone as efficiently as possible, and HMRlignan™ is the only lignan supplement with a proven dose response pharmacokinetic in this field,” says Robin Ward, Vice President of Marketing, Linnea Inc. “For the first time health-conscious individuals have an efficient method of supplementing lignan intake in the diet. This is important as maintaining circulating enterolactone levels can have a positive influence on health. In our human clinical study a dose of 10mg – 30mg was sufficient to raise enterolactone to levels that research shows to be beneficial.”

### **Lignans and Breast Health**

There has been extensive research demonstrating the correlation of enterolactone in women and the risk of breast cancer. In a case-control study to examine the association between serum enterolactone and risk of breast cancer in Finnish women researchers analyzed 194 breast cancer cases (68 pre-menopausal and 126 postmenopausal). The study found an inverse association between serum enterolactone and risk of breast cancer among both groups.<sup>1</sup> Proprietary research into hydroxymatairesinol (HMRlignan™) and enterolactone supports this finding. In a study conducted at the University of Turku, enterolactone was shown to inhibit the growth of 7,12-dimethylbenz(a)anthracene-induced mammary carcinomas in rats.<sup>2</sup> In another study HMRlignan™ was demonstrated to both inhibit tumor growth and to reduce tumor take rates.<sup>3</sup>

### **Lignans and Menopause**

Estrogen acts by binding to its receptors, and enterolactone may offer a natural selective estrogen-receptor modulator effect. By binding the estrogen receptor, enterolactone may exert an agonist or antagonist response. Depending on the concentration of endogenous estradiol and the distribution of estrogen receptors, enterolactone may act as either an estrogen receptor agonist or as an estrogen antagonist. When estrogen levels fall enterolactone may exert a weak estrogen-like effect (mimicking the presence of estrogen). Conversely, when estrogen levels are high, enterolactone will occupy and thus block estrogen receptors, thereby moderating the significant hormonal fluctuations that give rise to the typical symptoms of menopause. Healthy levels of circulating enterolactone may decrease both severity and occurrences of uncomfortable symptoms women experience.

“The good news for women is that the estrogenic activity of enterolactone is relatively weak and therefore the risk of unwanted effects due to adverse estrogenicity is minimal,” says Ward.

### **Lignans and Heart Health**

Research into diet and associated risk factors of cardiovascular disease has also been a focus of investigations in both men and women. The Kuopio Ischaemic Heart Disease Risk Factor Study, a population-based study of middle-aged Finnish men on the associations between serum

enterolactone level and the risk of coronary heart disease (CHD) and cardiovascular disease (CVD), concluded that high serum enterolactone level is dose-dependently positively associated with reduced CHD and CVD-related mortality<sup>4</sup>.

Again specific research into hydroxymatairesinol (HMRLignan™) and enterolactone lends support to these findings. In a Finnish study to evaluate evidence that low serum enterolactone concentration might be an independent risk factor for acute coronary events, researchers proposed that due to the bi-phenolic structure of enterolactone, along with the parent lignans, could act as an antioxidant and thus contribute to cardiovascular health. The study involving 100 participants tested the hypothesis that a low serum enterolactone concentration is associated with increased in vivo lipid peroxidation. In a multivariate analytical model, enterolactone persisted as a significant predictor after adjustment for vitamins and other variables, with the strongest associations with F2-isoprostanes. The study results support the hypothesis that low serum enterolactone concentration is associated with enhanced in vivo lipid peroxidation.<sup>5</sup> Proprietary research focusing on hydroxymatairesinol and enterolactone provides further pharmacological evidence on the benefits of HMRLignan™ for heart health. In vitro tests show HMRLignan™ to be a strong antioxidant more or equipotent to Trolox, to incorporate into isolated LDL fractions, and to protect from copper-induced LDL oxidation in vitro.<sup>3</sup> Ongoing research also indicates the capacity of HMRLignan™ and enterolactone to modulate inflammatory reactions in heart health.

### **About Linnea**

From its headquarters and manufacturing facility in Locarno, Switzerland, Linnea specializes in the manufacture of botanical extracts and phytochemicals, and is a leading supplier to the pharmaceutical, dietary supplement and cosmetic industries. HMRLignan™ is a proprietary, patent protected, product manufactured by Linnea SA. The company's U.S. office, Linnea Inc., is located in Easton, Pennsylvania. For more information about HMRLignan™, visit our Web site at [www.hmrlignan.com](http://www.hmrlignan.com) or call 1-888-253-0044.

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