

Patient: **SAMPLE**  
**PATIENT**

**Order Number:**

Completed: February 22, 2008

Age: 59

Received: February 20, 2008

Sex: F

Collected: February 14, 2008

MRN:

<b>Progesterone</b>		
Hormone	Reference Range	Reference Range
Progesterone	0.61	0.30-1.13 ng/mL

<b>Binding Proteins</b>		
Hormone	Reference Range	Reference Range
Sex Hormone Binding Globulin	80	18-114 nmol/L

<b>Estrogens</b>		
Hormone	Reference Range	Reference Range
Estrone Sulfate (E1S)	2.18	0.56-2.67 ng/mL
Estrone (E1)	85	20-95 pg/mL
Estradiol (E2)	33	20-160 pg/mL
Estriol (E3)	113	<= 80 pg/mL

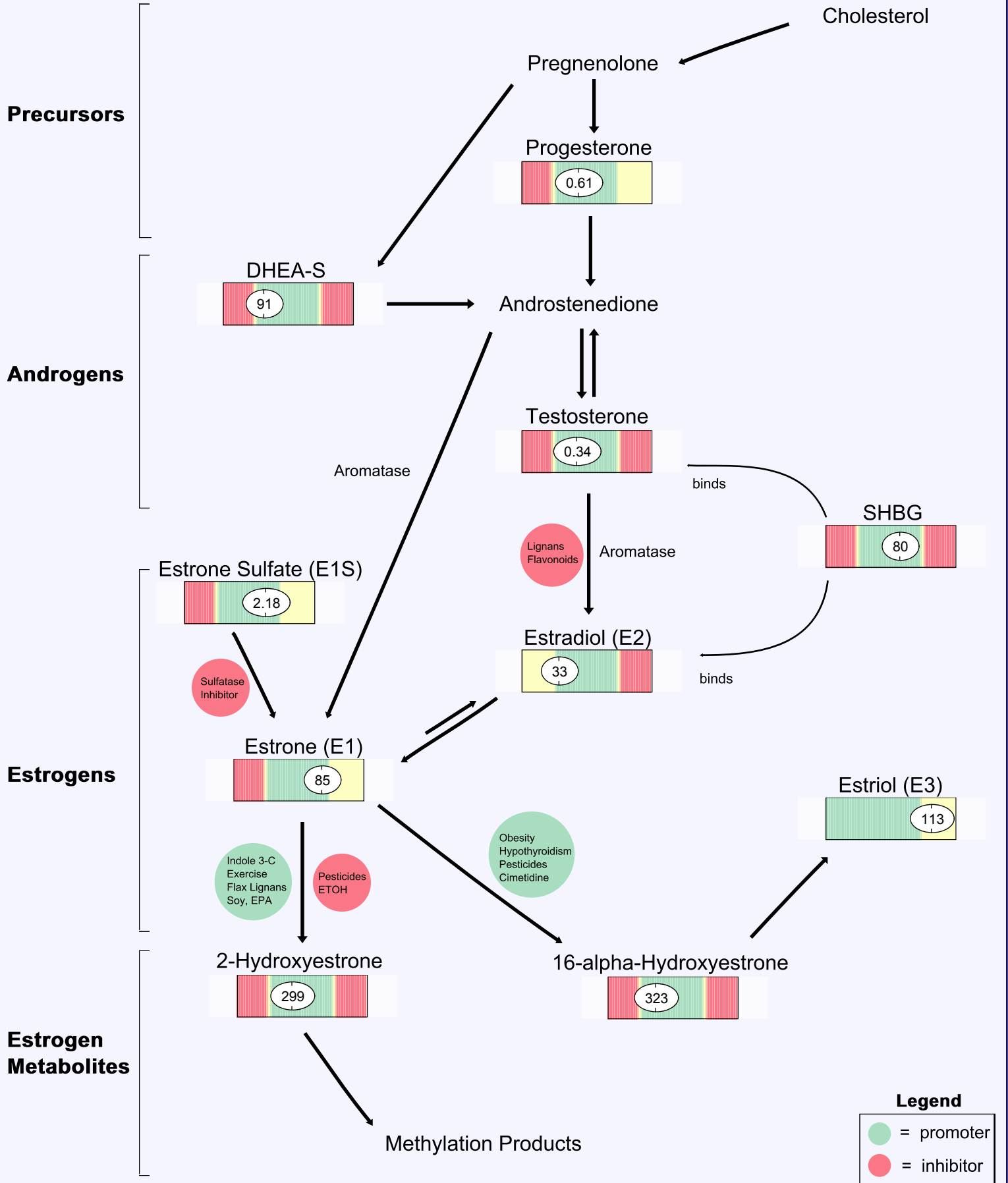
<b>Androgens</b>		
Hormone	Reference Range	Reference Range
DHEA-S	91	35-430 mcg/dL
Testosterone	0.34	0.10-0.80 ng/mL
Free Androgen Index	1.47	0.22-5.78

<b>Estrogen Metabolism</b>		
Hormone	Reference Range	Reference Range
2-Hydroxyestrone	299	112-656 pg/mL
16 $\alpha$ -Hydroxyestrone	323	213-680 pg/mL
2:16 $\alpha$ -Hydroxy-Estrone Ratio	0.93	0.40-1.40

### *Reference Range Information*

Reference ranges for the estrogen metabolites were determined with serum samples from women with a normal 2:16 $\alpha$ -Hydroxyestrone Ratio. Other reference ranges were determined with follicular serum samples from premenopausal women who were not using hormone replacement therapy. These ranges serve as clinical guidelines to observe changes due to hormone replacement. However, each individual is unique and treatment should be tailored to the patient's clinical picture.

### Steroidogenic Pathway



Analyte	Premenopausal follicular	Premenopausal luteal	Unsupplemented Menopausal	Patient Results
<b>Estrone Sulfate</b> (ng/mL)	0.56 - 2.67	0.75 - 4.28	0.23 - 1.40	2.18
<b>Estrone</b> (pg/mL)	20 - 95	28 - 163	12 - 41	85
<b>Estradiol</b> (pg/mL)	20 - 160	27 - 246	20 - 24	33
<b>Estriol</b> (pg/mL)	<= 80	<= 80	<= 80	113
<b>Progesterone</b> (ng/mL)	0.30 - 1.13	0.95 - 21.00	0.30 - 0.64	0.61
<b>Testosterone</b> (ng/mL)	0.10 - 0.80	0.10 - 0.80	0.07 - 0.46	0.34
<b>DHEA-s</b> (mcg/dL)	35 - 430	35 - 430	30 - 202	91

## Commentary

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. All assays are cleared by the U.S. Food and Drug Administration unless otherwise noted with

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Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

### Women's Hormonal Health Assessment (Menopausal Patient)

#### Progesterone

**Progesterone** is within the reference range. Progesterone is a steroid hormone that is produced primarily by the corpus luteum in premenopausal women. In menopause, the adrenal glands become the primary source of progesterone, which may fluctuate in response to ACTH secretion by the pituitary. As this hormone reduces the proliferative effects of estrogens on the endometrium, adequate levels are particularly important with exogenous estrogen administration.

#### Binding Proteins

**Sex hormone-binding globulin (SHBG)** is within the reference range. SHBG serves as a protein carrier for steroid hormones, with a binding affinity in the order of dihydrotestosterone > testosterone > estradiol. The biologic effects of these steroid hormones (especially testosterone) are largely determined by the unbound portion. Thus, SHBG exerts a major regulatory effect on circulating levels of these steroids.

#### Androgens

**Dehydroepiandrosterone sulfate (DHEA-S)** is within the reference range. DHEA-S circulates in a higher concentration than any other steroid, is derived from the adrenal gland in response to ACTH, and is the storage form for DHEA. This hormone serves as a precursor to other androgens, which may in turn be enzymatically converted to estrogens via aromatase activity in various tissues, particularly adipose, skin, and bone. Since much of the bone-protective effect of estrogen appears to be dependent on aromatization from androgens within bone tissue itself, DHEA-S may be particularly important in the menopausal woman. DHEA-S also plays an important role in thyroid function, immune regulation, maintenance of libido and lean body mass, insulin sensitivity, and balancing the body's stress response. DHEA-S levels peak between the ages of 20 and 30 years, thereafter decreasing markedly, along with downstream androgens and estrogens.

Low normal levels of DHEA-S have been observed in numerous conditions including chronic stress, depression, obesity, impaired immunity, rheumatoid arthritis, lupus, and cardiovascular disease. In light of such correlations, it may be prudent to regard low normal levels as clinically significant in patients whose clinical picture supports it.

**Testosterone** is within the reference range. In the menopausal woman, testosterone is derived from both adrenal and ovarian activity, although production in the latter decreases in comparison to premenopausal years. In peripheral tissues, particularly adipose, testosterone is converted into estradiol via the aromatase enzyme. Normal levels provide protection against osteoporosis, and help maintain libido and lean muscle mass. Testosterone has very strong binding with SHBG; therefore, the higher the SHBG, the lower the amount of bioavailable testosterone. This relationship is reflected in the Free Androgen Index.

## Commentary

The **Free Androgen Index** is described in the literature and provides a calculated indicator of unbound (bioavailable) testosterone. While not representing ALL of the androgenic effects present, the FAI is a reasonable means to determine the effects of androgens in women. This value is calculated by multiplying the testosterone value by a unit conversion factor, dividing by the SHBG value, and multiplying by 100. The FAI may be particularly significant in relation to PCOS, hirsutism, acne, and breast cancer.

### Estrogens

**Estrone sulfate (E1-S)** is within the reference range.

Estrone sulfate is the most abundant circulating estrogen in non-pregnant women. Because E1-S is unable to bind to the estrogen receptor, it is biologically inactive. However, E1-S serves as an important reservoir for active estrogens, especially after menopause when the ovary is no longer the primary source of estrogens. E1-S is converted to estrone within estrogen target tissues such as ovary, placenta, skin, brain, endometrium, bone, and blood. Estrone can then be converted to the more potent estradiol, or be re-sulfated to inactive E1-S.

Normal levels of E1S suggest normal sulfation activity and reserve of estrogens. Together, E1-S, estrone, and estradiol provide an approximation of total estrogenicity in the body.

**Estrone (E1)** is within the reference range. Estrone is the second most potent estrogen after estradiol and is derived from either adrenal androstenedione via aromatization in peripheral tissues such as adipose, or from estradiol (reversible reaction). Although total estrogens decline in menopause, estrone becomes the predominant circulating estrogen. Estrone is bound primarily to albumin rather than SHBG, and may be processed via either the 2- or 16alpha-hydroxylation pathways to form 2-hydroxyestrone or 16alpha-hydroxyestrone, respectively.

Normal levels of estrone imply adequate conversion from aromatase activity or HRT supplementation. Secondary metabolism should be checked in the "Estrogen Metabolism" section of the report.

**Estradiol (E2)** is within the reference range. Estradiol is the most potent estrogen and is the major estrogen secreted by the ovaries in a premenopausal woman. In the postmenopausal woman, estradiol arises either from estrone (reversible reaction) or from testosterone via aromatization in peripheral tissues such as adipose. Although more potent than estrone, estradiol is the less plentiful of the two estrogens in postmenopausal women.

Estrogens stimulate growth and development of tissues related to female reproduction such as the breasts, vagina and uterus. Estrogens in postmenopausal women assist with maintenance of bone integrity and vascular smooth muscle tone, collagen production, brain activity, and the maintenance of normal vaginal epithelial function.

**Estriol (E3)** is above the reference range. The least potent of the estrogens, E3 levels are traditionally used clinically to gauge the viability of pregnancies. In the context of this profile, estriol is least likely to be associated with high-estrogen problems (e.g. breast cancer), and is generally viewed as a "protective" estrogen. Conversion of 16alpha-hydroxyestrone to estriol is important to consider.

If the patient is taking a "Bi-Est" or "Tri-Est" preparation, an elevated estriol is not unusual. The clinician will be reminded that reference ranges in this profile are premenopausal follicular, in which estriol comprises a small portion of the total estrogen pool.

High estriol implies a potential for elevated 16alpha-hydroxyestrone, a very potent estrogen that is associated with increased risk of breast cancer. There appears to be an association of elevated estriol and elevated 16alpha-hydroxyestrone in patients with systemic lupus erythematosus, implying shifted metabolism in that condition.

## Commentary

### Estrogen Metabolism

**2-Hydroxyestrone (2-OHE1)** levels were found to be within the reference range. This metabolite of estrone has been called the "good" estrogen, and appears to represent a beneficial direction in estrogen metabolism. Normal levels of the 2-OHE1 imply a balanced metabolism and generally may be maintained through a lifestyle of good diet, exercise and reasonable intake of EPA, cruciferous vegetables, and flaxseeds. Changes in 2-OHE1 may be particularly important for women to monitor as their hormone status changes due to contraceptives, estrogen replacement therapies, diet, or exercise regimen.

**16alpha-Hydroxyestrone (16alpha-OHE1)** levels are within the reference range. As this metabolite of estrone may be associated with estrogen-dependent diseases, such as lupus and breast cancer, normal or low levels are good to observe. There are means to influence and perhaps reduce the production of this metabolite; exercise, intake of soy and cruciferous vegetables, and fish oil (EPA) all appear to be of potential benefit at keeping the levels normal or low.

The **2:16alpha-Hydroxyestrone ratio** appears from the literature to be an important gauge of estrogen metabolism. In general, the higher the ratio, the less association there is with estrogen-dependent diseases such as breast cancer and lupus, and the more likely the person has a beneficial hormone metabolism. A 2:16alpha-hydroxyestrone ratio in serum greater than 0.4 is generally thought to be beneficial. There are numerous modifiers of this value, most of which induce changes in the level of 2-OHE1. These include intake of indole-3-carbinols from cruciferous vegetables, flaxseed, soy, omega-3 fatty acids, and vigorous exercise. All are shown to improve the levels of 2-OHE1 in most individuals. It is to be emphasized that some individuals in clinical studies have exhibited a paradoxical response to treatments that would typically raise the 2-OHE1 levels. Therefore, follow-up testing after treatment is strongly suggested.

There may be an increased likelihood of osteoporosis with excessive 2-OHE1 production. It is important to note that the ideal upper limit of 2-OHE1 is not apparent from the existing literature. Attention to bone loss processes in the urine is perhaps warranted in individuals with a very high 2:16alpha-hydroxyestrone ratio.