

# Estrogen Metabolism Assessment (Urine)



63 Zillicoa Street  
Asheville, NC 28801  
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Patient:  
DOB:  
Sex: F  
MRN:

**Order Number:**

Completed:  
Received:  
Collected:

Methodology: LC-MS/MS; Results normalized to creatinine

## Estrogens

### Estrogens

### Reference Range

16 $\alpha$ -Hydroxyestrone (16 $\alpha$ -OH E1)*	5.0	0.5-8.9 mcg/g Creat.
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\*Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	0.5-8.9 mcg/g Creat.
Menopause	0.4-7.7 mcg/g Creat.
Male	<=2.0 mcg/g Creat.

2-Hydroxyestrone + 2-Hydroxyestradiol [2-OH(E1+E2)] *	3.8	1.3-36.3 mcg/g Creat.
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\* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	1.3-36.3 mcg/g Creat.
Menopause	0.9-43.8 mcg/g Creat.
Male	0.7-12.5 mcg/g Creat.

2-OH(E1+E2) / 16 $\alpha$ -OHE1*	0.8	0.3-13.7
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\* Premenopause (luteal) reference range shown

Reference Ranges	
Premenopause	0.3-13.7
Menopause	0.3-15.1
Male	0.8-12.9

Creatinine	51.54	27.00-248.00 mg/dL
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## Lab Comments

The performance characteristics of all assays have been verified by Genova Diagnostics, Inc. Unless otherwise noted with ♦, the assay has not been cleared by the U.S. Food and Drug Administration.

Please note analysis of estrogens and estrogen metabolites is now performed using LC/MS/MS. The reference ranges for these biomarkers have been updated.

**Commentary**

## Commentary

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.

### Estrogen Metabolites

Estrogens are metabolized by two main pathways: (1) formation of the catechol estrogens 2-hydroxyestrone/estradiol (2-OHE1/E2) via the CYP1A1 pathway and 4-hydroxyestrone/estradiol (4-OHE1/E2) via the CYP1B1 pathway; and (2) formation of 16 $\alpha$ -hydroxyestrone (16 $\alpha$ -OHE1) via the CYP3A4 pathway.

### 2/16 Ratio and Hydroxylation pathways

2/16 Ratio - The clinical utility of the ratio of 2-hydroxyestrone (2-OHE1) to 16 $\alpha$ -hydroxyestrone (16 $\alpha$ -OHE1) – the 2/16 ratio or Estrogen Metabolite Ratio (EMR) – historically reported lower 2/16 ratio levels among breast cancer cases compared to controls (particularly in premenopausal women). Recent studies have been mixed: there appears to be no strong evidence in the literature that a higher urinary 2/16 ratio protects postmenopausal women from breast cancer, and only weak evidence of a protective effect in premenopausal women.

Higher 2-OH (E1+E2)/16 $\alpha$  –OH ratios in males have been associated with reduced risk of prostate cancer.

**2-OH (E1+E2)** - While traditional 2/16 ratio clinical utility may not be as robust as previously thought, a majority of findings indicate that metabolism of parent estrogens through 2-hydroxylation (independent of any relationship to 16 $\alpha$ -OHE1) may be considered as a benign or even protective pathway. (Of note: one study found increased breast cancer risk with higher 2-OH levels, but only in a small subgroup of ER-/PR- cases.)

Studies suggest that women with predominant metabolism through the 2-hydroxyl pathway have accelerated postmenopausal bone loss and lower BMD compared to those with predominant 16 $\alpha$ -hydroxylation who appear to have reduced risk of bone loss. Increased 2- hydroxylation has been noted in women with a positive family history of osteoporosis suggesting that increased risk of osteoporosis in those with a family history may be related to inherited differences in estrogen metabolism.

**16 $\alpha$ -OH** - Recent findings in the peer-reviewed literature are mixed, with some studies finding an association with increased risk (cancers of the cervix, breast, endometrium, and head and neck, as well as in people with tumors related to the human papilloma virus), but many finding no significant association.