CARDIOLOGY
NEPHROLOGY
BONE
ONCOLOGY
AUTOIMMUNITY
INFECTIOUS DISEASE
DIABETES

LIAISON®

25 OH Vitamin D TOTAL Assay

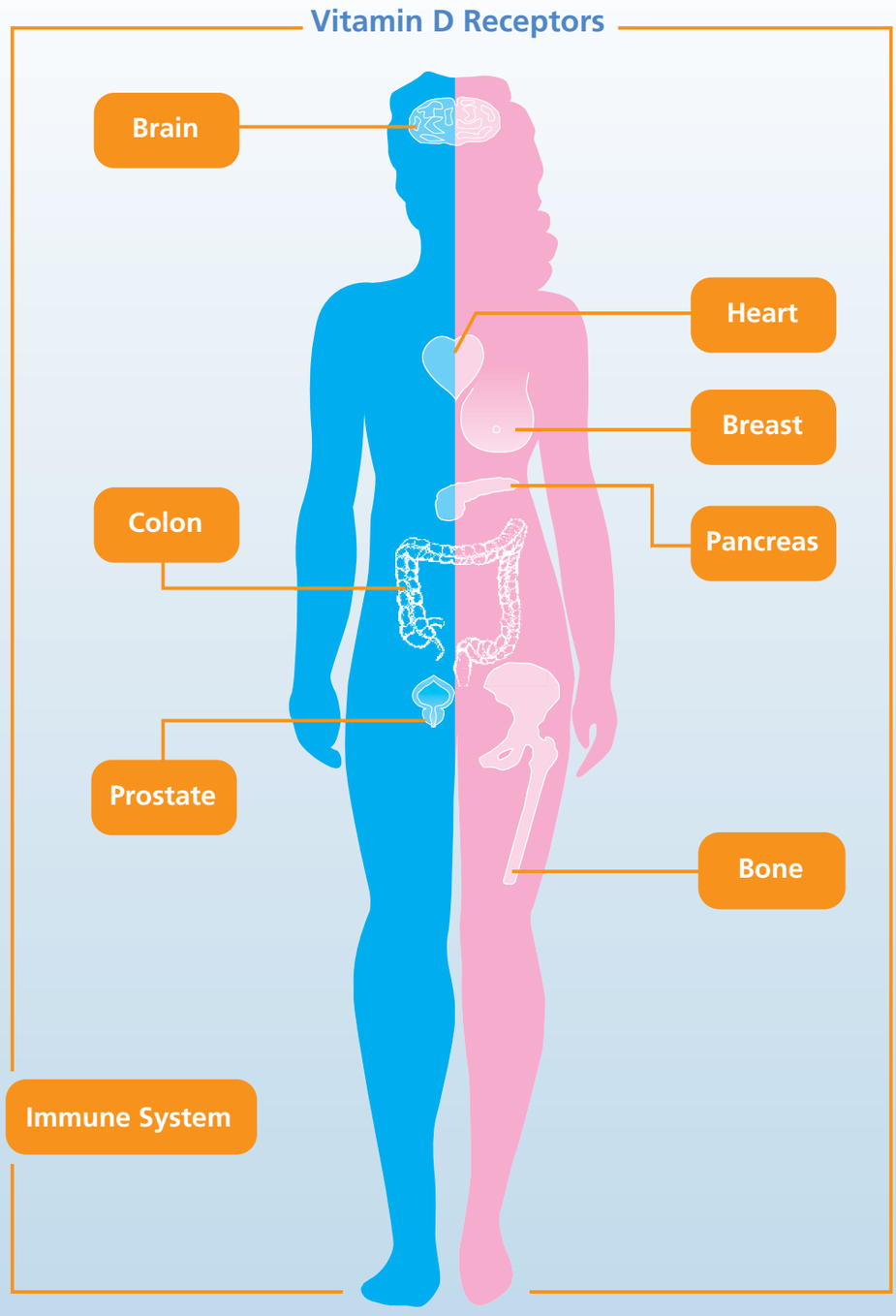
25-hydroxyvitamin D: from bone and mineral to general health marker

DiaSorin

The Diagnostic Specialist

FOR OUTSIDE THE US ONLY

25-hydroxyvitamin D: i
to general



r from bone and mineral
n health marker

The role of vitamin D in regulating circulating levels of calcium and phosphorus to ensure normal bone mineralization is well known.

Emerging evidence correlates insufficient levels of vitamin D to an increased risk of developing non-skeletal pathologies: cardiovascular diseases, hypertension, cancer, diabetes, multiple sclerosis, rheumatoid arthritis, infectious diseases.

The diverse effects of vitamin D are mediated by receptors that regulate more than 200 genes. Besides the receptors present in the intestine and the bone, vitamin D receptors have been identified in brain, prostate, breast, colon, immune cells, vascular smooth muscle and cardiomyocytes. (1,2)

Maintaining sufficient vitamin D levels is therefore key to maintain good general health.
Vitamin D status is assessed by measuring the serum concentration of 25-hydroxyvitamin D:

Deficiency	**< 10 ng/mL**	**(0-25 nmol/L)**
Insufficiency	**10-30 ng/mL**	**(25-75 nmol/L)**
Sufficiency	**30-100 ng/mL**	**(75-250 nmol/L)**
Toxicity	**> 100 ng /mL**	**(>250 nmol/L)**

It has been estimated that 1 billion people worldwide do not reach the minimum optimal concentration of 30 ng/mL. (1)

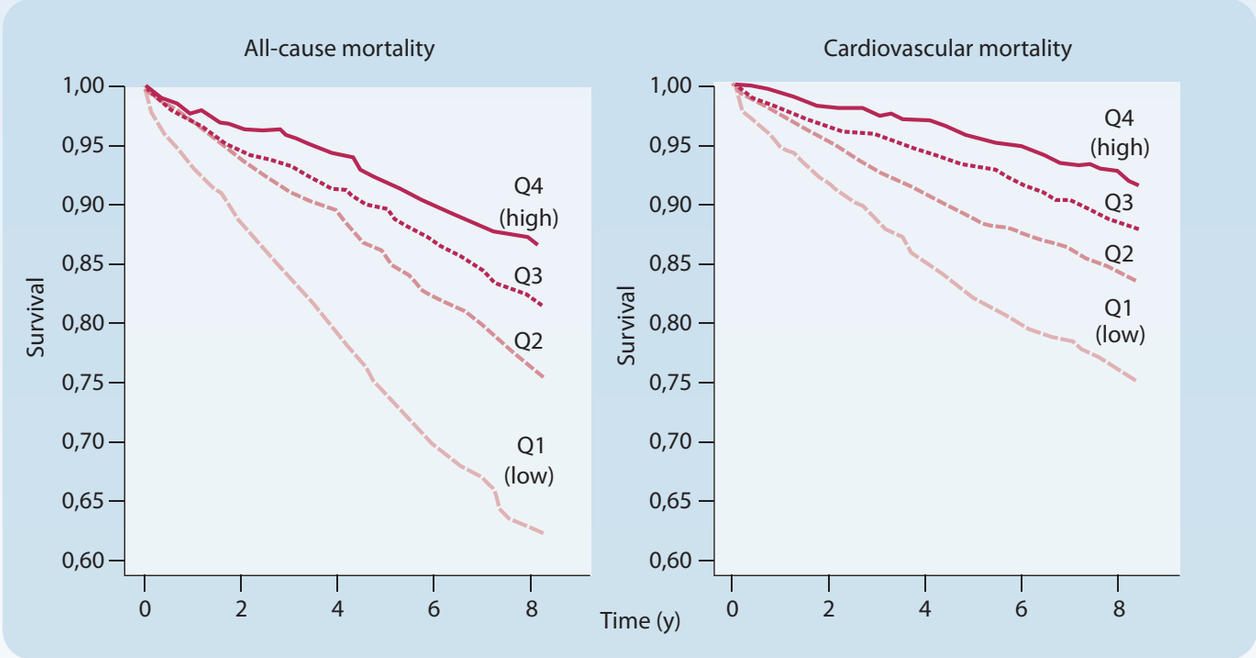
1) Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-81
2) Wang TJ et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation 2008;117:503-511

An increasing number of studies associate vitamin D insufficiency with a higher risk of developing several pathologies

A prospective study in which 1739 participants without prior cardiovascular disease were followed-up for 5 years showed that individuals with hypertension and 25(OH) vitamin D levels <15 ng/mL had a 2-fold risk of cardiovascular events compared to those with levels >15 ng/mL. (2)

An analysis of 454 men, who were free of diagnosed cardiovascular disease at baseline and developed myocardial infarction or coronary heart disease during 10 years of follow-up, and 900 controls indicated that the risk of myocardial infarction was double for individuals with insufficient levels of 25(OH) vitamin D (<15 ng/mL) compared to sufficient levels (>30 ng/mL). (3)

A 7-year follow-up study of 3258 patients referred for coronary angiography showed that decreasing 25(OH) vitamin D levels (Q1 = 7.6 ng/mL, Q2 = 13.3 ng/mL, Q3 =18.9 ng/mL, Q4 = 28.4 ng/mL) were associated with increasing risk for all-cause and cardiovascular mortality. (4)



3) Giovannucci E et al. 25-Hydroxyvitamin D and risk of myocardial infarction in men. Arch Intern Med 2008;168(11):1174-1180

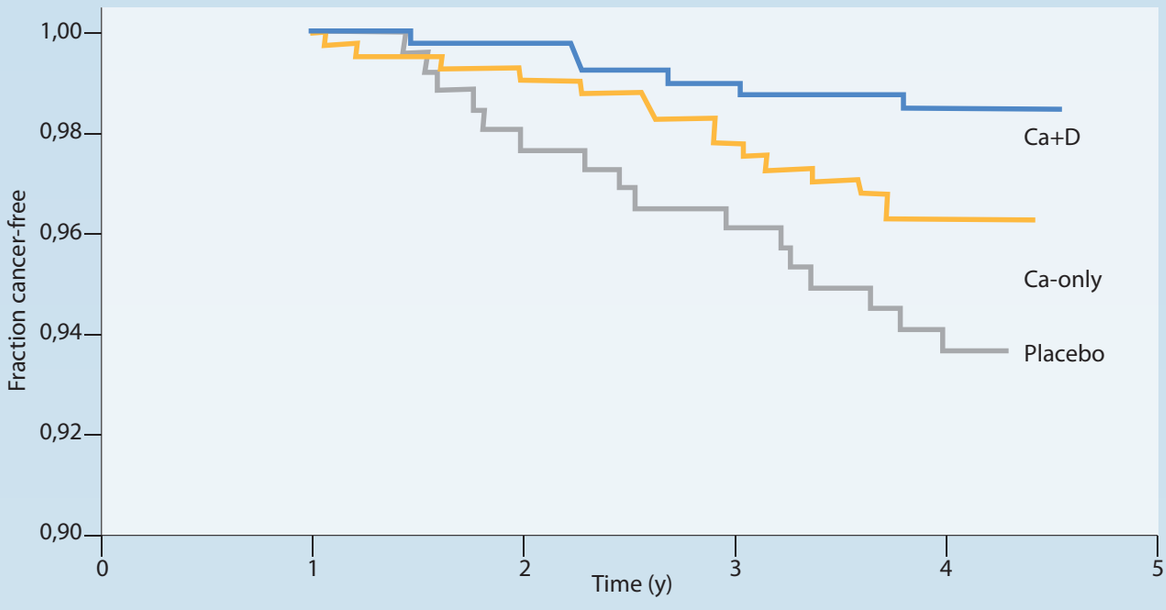
4) Dobnig H et al. Independent association of low serum 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D levels with all-cause and cardiovascular mortality. Arch Intern Med 2008;168(12):1340-1349

An increasing number of studies associate vitamin D insufficiency with a higher risk of developing several pathologies

A pooled analysis of two studies with 880 cases of breast cancer and 880 controls demonstrated that individuals with serum 25(OH) vitamin D of approximately 52 ng/mL had 50% lower risk of breast cancer than those with levels <13 ng/mL. (5)

An analysis of 1394 post-menopausal breast cancer cases and 1365 controls suggested that serum 25(OH) vitamin D concentration was significantly inversely associated with breast cancer risk, particularly at levels <20 ng/mL. (6)

A 4-year trial including 1085 healthy women supplemented with placebo, calcium or calcium + vitamin D showed that vitamin D supplementation reduced by 77% the relative risk of developing cancer. (7)



5) Garland CF et al. Vitamin D and prevention of breast cancer: pooled analysis. J Steroid Biochem Mol Biol 2007;103:708-711

6) Abbas S et al. Serum 25-hydroxyvitamin D and risk of post-menopausal breast cancer - Results of a large case-control study. Carcinogenesis 2008;29(1):93-99

7) Lappe JM et al. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. Am J Clin Nutr 2007;85:1586-91

An increasing nu
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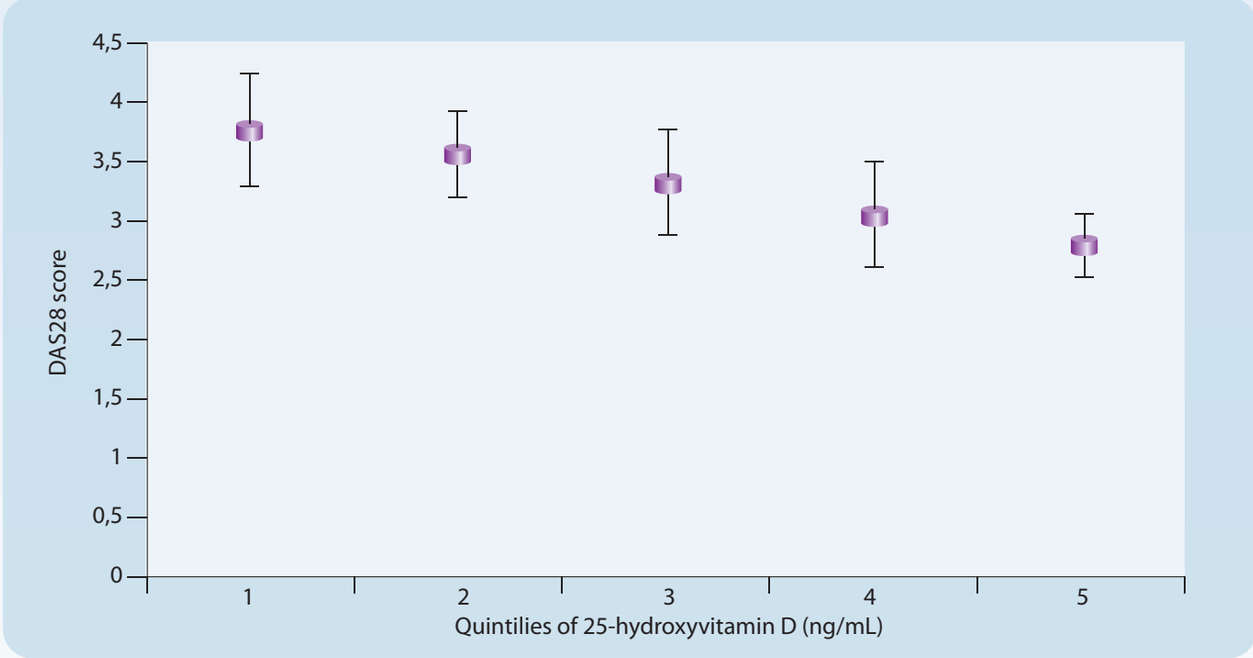
- The risk of multiple sclerosis in a white population of 148 patients and 296 controls was demonstrated to be 51% lower for individuals with 25(OH) vitamin D levels >40 ng/mL compared to levels <30 ng/mL. (8)

- A study including 103 patients and 110 controls showed that for every 4 ng/mL increase of serum 25(OH) vitamin D the odds of multiple sclerosis were reduced by 19% in women. (9)

- In a population of 206 patients with early inflammatory polyarthritis, an inverse relationship between 25(OH) vitamin D levels and the Disease Activity Score 28-joint assessment was found: each 10 ng/mL increase in 25(OH) vitamin D was associated with a decrease in the DAS28 score of 0.3. (10)



8) Munger KL et al. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. J Am Med Assoc 2006;296(23): 2832-2838

9) Kragt J et al. Higher levels of 25-hydroxyvitamin D are associated with a lower incidence of multiple sclerosis only in women. Mult Scler 2009;15(1):9-15

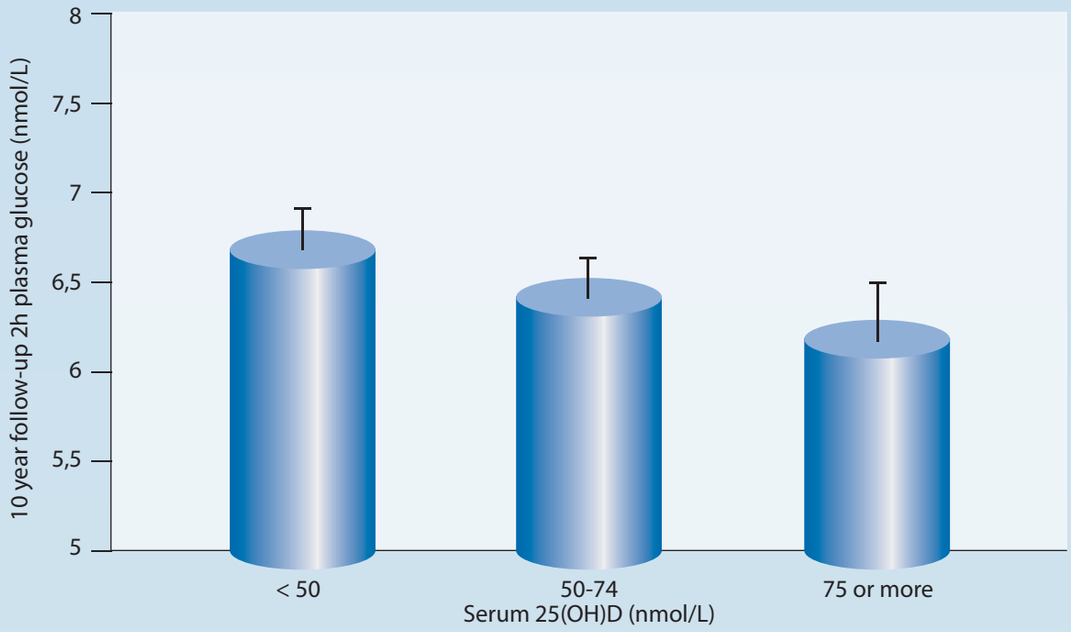
10) Patel S et al. Association between serum vitamin D metabolite levels and disease activity in patients with early inflammatory polyarthritis. Arthritis Rheum 2007;56(7):2143-2149

umber of studies fficiency with a higher risk veral pathologies

In a cohort of 10366 children, vitamin D supplementation with daily doses of 2000 IU was associated with a 78% reduced risk of developing type 1 diabetes compared to lower doses. (11)

A meta-analysis of 4 studies with a total of 1429 cases and 5026 controls indicated that children receiving vitamin D supplements had a 29% reduction in the risk of developing type 1 diabetes compared to non-supplemented children. (12)

A 10 years follow-up of 524 non-diabetic adults demonstrated and inverse association between baseline serum 25(OH) vitamin D levels and future hyperglycemia and insulin resistance. (13)



11) Hypponen E et al. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. Lancet 2001;358(9292): 1500-3

12) Zipitis CS et al. Vitamin D supplementation in early childhood and risk of type 1 diabetes: a systematic review and meta-analysis. Arch Dis Child 2008;93:512-517

13) Forouhi NG et al. Baseline serum 25-hydroxyvitamin D is predictive of future glycemic status and insulin resistance: the Medical Research Council Ely Prospective Study 1990-2000. Diabetes 2008;57(10):2619-25

Knowing and monitor
levels is key to maintain

An analysis of studies demonstrating the role of vitamin D in the prevention of several pathologies suggests that reaching and maintaining 25-hydroxyvitamin D levels above 30 ng/mL, preferably around 36-40 ng/mL, is key to maintain good health. (14)

Such levels include the metabolites of both forms of vitamin D: D_2 and D_3. Whereas vitamin D_3 is produced by the skin upon exposure to sunlight, both D_2 and D_3 are contained in food sources.

In most countries, vitamin D supplements containing D_2 or D_3 are available, which can help compensate the insufficient dietary intake and sun exposure.

Correct clinical decisions are based on the assessment of 25-hydroxyvitamin D TOTAL levels.

Accurate assessment of vitamin D status relies on the measurement of 25-hydroxyvitamin D TOTAL levels (25-hydroxyvitamin D_2 + 25-hydroxyvitamin D_3), which can be compared with the optimal levels recommended by vitamin D experts.

Two separate values for 25(OH) vitamin D_2 and 25(OH) vitamin D_3 could lead to erroneously interpret low levels of one of the two metabolites as indicative of vitamin D insufficiency even when the sum is within the sufficiency range. (15)

Measuring 25-hydroxyvitamin D TOTAL levels is important to monitor treatment. Clinical cases of supplementation with vitamin D_2 have been reported in which an assay that was only able to detect 25-hydroxyvitamin D_3 was used for patient follow-up. The inability to measure the increase in 25-hydroxyvitamin D TOTAL levels upon supplementation can cause overtreatment and lead to further expensive and stressful studies. (16)

14) Bischoff-Ferrari HA et al. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006;84:18-28

15) Binkley N et al. Laboratory reporting of 25-hydroxyvitamin D results: potential for clinical misinterpretation. Clin Chem 2006;52(11):2124-2125

16) Cavalier E et al. Case report. Serum vitamin D measurement may not reflect what you give to your patients. J Bone Miner Res 2008;23:1864-1865

ing vitamin D TOTAL good general health

LIAISON®
25 OH Vitamin D **TOTAL**
Assay

Since 1985, DiaSorin has provided laboratories with assays that accurately measure 25-hydroxyvitamin D total levels, thanks to antibodies that are co-specific for 25-hydroxyvitamin D_2 and 25-hydroxyvitamin D_3.

The ^{125}I RIA 25-hydroxyvitamin D assay has set the standard for the clinical diagnosis of nutritional vitamin D deficiency and has been used in most studies correlating it to the risk of developing various diseases. (17)

The LIAISON 25 OH Vitamin D TOTAL Assay ensures the same specificity as the RIA assay, being based on the same antibody, with a much higher throughput (>100 results/hour).

The LIAISON 25 OH Vitamin D TOTAL Assay represents the only fully automated assay measuring 25-hydroxyvitamin D total levels and allows accurate and quick determination and monitoring of vitamin D status.

17) Hollis BW. Measuring 25-hydroxyvitamin D in a clinical environment: challenges and needs. Am J Clin Nutr 2008; 88(2):507S-510S

Summary

- The function of vitamin D is not limited to maintaining normal bone mineralization, but involves different organs and tissues containing specific receptors.
- Maintaining sufficient levels of 25-hydroxyvitamin D (>30 ng/mL) helps preventing several pathologies and maintaining good general health.
- Correct clinical decisions are based on the assessment of 25-hydroxyvitamin D TOTAL (D_2 + D_3) levels.
- The DiaSorin assays have been used to define the 25-hydroxyvitamin D reference levels.
- The LIAISON 25 OH Vitamin D TOTAL Assay, measuring 25-hydroxyvitamin D total levels on a fully automated platform, allows accurate and quick determination of vitamin D status and effective therapy monitoring.

LIAISON®
25 OH Vitamin D **TOTAL** Assay

- Recognizes 100% 25 (OH) vitamin D_2 and 25 (OH) vitamin D_3
- Excellent correlation with the DiaSorin 25-hydroxyvitamin D RIA assay, which has been used to define the reference levels.
- Advanced chemiluminescence technology with paramagnetic particles separation to achieve the best assay sensitivity and precision
- No solvent extraction
- Dynamic range: 4.0 – 150 ng/mL
- Functional sensitivity: ≤ 4.0 ng/mL
- First result in 35 minutes, throughput > 100 results/hour

LIAISON® 25 OH Vitamin D TOTAL Assay (code 310600)
LIAISON® 25 OH Vitamin D TOTAL Control Set (code 310601)
LIAISON® 25 OH Vitamin D TOTAL Specimen Diluent Set (code 310602)

DiaSorin S.p.A.
Via Crescentino
13040 Saluggia (VC) – Italy
Tel. +39.0161.487526
Fax: +39.0161.487670
www.diasorin.com – E-mail: info@diasorin.it

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