Free Thyroxine (fT4) and Free Triiodothyronine (fT3)	
Description	Free thyroxine (fT4) and free triiodothyronine (fT3) are the 2 biologically active thyroid hormones.
Indication	As part of the complete investigation of the hypothalamic-pituitary-thyroid axis.
Additional Info	The use of haemolyzed or lipaemic samples is not recommended. Apart from heparin, most blood-collection-tube additives have little if any effect on the performance of isotopic assays. Patients on heparin therapy may have increased free fatty acids in stored serum samples as a result of heparin-induced lipoprotein lipase activity. These free fatty acids displace thyroxine (T4) from TBG and may cause an artifactual increase in the FT4 concentration. Drugs such as furosemide, disalicylic acid, phenytoin, and carbamazepine, which displace T4 from thyroid binding globulin (TBG), cause dilution artifacts in fT4 assays which dilute samples as part of the analytical procedure. Abnormal binding proteins can cause artifactual high or low results. Examples include autoantibodies, rheumatoid factor, and familial dysalbuminaemic hyperthyroxinaemia. Nonspecific interference by ruthenium cross-linking causing artifactual elevation of results has been observed in the Roche E170 electrochemiluminescent one-step assays for $fT_{T4}$and fT3.
Concurrent Tests	May be performed as part of the thyroid function tests (TFTs).
Dietary Requirements	N/A
Interpretation	For correct interpretation, it is important to note that a number of factors (e.g., age, gender, pregnancy) can alter the concentration of free thyroid hormones under physiological conditions. It is important to recognize that fT4 and total T4 population-based reference intervals are wide when compared to the narrow reference interval for individuals. If the hypothalamic-pituitary axis is normal, TSH is generally a more sensitive indicator of thyroid status than fT4/fT3. fT4 and fT3 should be combined with TSH results for interpretation. Low TSH and increased fT4 and or fT3 indicates hyperthyroidism elevated TSH and decreased fT4 and fT3 indicates primary hypothyroidism. Subclinical thyroid disease has been defined as when a patient has fT4and or fT3 within the population reference interval but an abnormal TSH concentration. One explanation for sub-clinical thyroid disease is the narrow intra-individual biological variation. When the thyroid function spontaneously changes or the level of thyroid hormone therapy is altered, the pituitary TSH response may require several weeks for full expression. The “time lag” needed to achieve full TSH response to changes in circulating fT4 (and fT3) requires a minimum of 4 and as long as 12 weeks to occur. A useful follow-up test for those with a confirmed elevation of TSH (sub clinical hypothyroid) is measurement of thyroid peroxidase antibodies. Because of the high prevalence of both thyroid disease and non-thyroidal illness (NTI) in hospitalized patients, newer schemes for testing follow different approaches for healthy populations (e.g., newborns, elderly subjects) and ambulatory subjects compared to hospitalized patients. Hence caution is advised in the interpretation of

	thyroid-function test results in hospitalized or acutely ill patients, since the results can be misleading. Besides considerable physiological variations due to age, pregnancy, and other conditions, free thyroid hormone results can be difficult to interpret because of patient overall disease state, medications, and other less common factors. *NTI* refers to the anomaly of patients who display abnormal results in their thyroid function tests but do not actually appear to suffer directly from thyroid disease. These include those patients who are mildly to severely unwell or stressed and those to whom certain pharmacological agents have been administered. Among the thyroid abnormalities, most prominent are low serum T3 (and often elevated reverse T3) concentrations. In patients suffering from more severe NTI, both serum fT3 and fT4 are depressed, and this condition was originally described as *euthyroid sick syndrome*. The decrease in serum fT4 may be severe and can indicate a poor outcome. In mild cases of NTI, serum free and total T4 both tend to be higher than normal. NTI patients present two types of diagnostic challenges. One is differentiation of abnormal thyroid results caused by NTI from those caused by a treatable thyroid disorder. The other is the treatment and monitoring of thyroid patients, particularly those with hypothyroidism whose disease is obscured by the presence of NTI.
Collection Conditions	The preferred specimen is a serum sample that has been removed from the clot as rapidly as possible. Fresh serum samples may be stored at room temperature for up to 1 week without appreciable changes, but storage at 4°C is preferred if the test is not performed within 24 hours.
Frequency of testing	Contact laboratory, disease and treatment specific.