
Element i+™ Total T4 Product Bulletin

Introduction

Total thyroxine (T4) measures the major hormone secreted by the thyroid gland, which plays a central role in metabolic regulation. Total T4 measurement is a core component of veterinary thyroid testing. In dogs, it is widely used as a screening test for hypothyroidism; in cats, it is a key test in the evaluation and diagnosis of hyperthyroidism.

Assay Overview

Intended use: Quantitative determination of Total T4 in canine and feline serum or lithium heparin plasma.

Reportable range: 0.7–20.0 µg/dL (9–257 nmol/L). The assay is used as an aid in screening for canine hypothyroidism, feline hyperthyroidism, and for monitoring therapeutic response.

Materials and Methods

A method comparison study was performed in accordance with CLSI EPO9c guidelines using patient samples spanning the assay reportable range (approximately 0.7–20.0 µg/dL). A total of 337 canine and 250 feline samples were tested on both the Element i+ Total T4 assay and a commercially available reference immunoassay (IMMULITE® 2000).

Statistical evaluation included Passing–Bablok regression to assess proportional and constant bias between methods across the measuring interval, along with calculation of slopes, intercepts, and associated confidence intervals. In addition, Bland–Altman difference analysis was used to evaluate mean bias and limits of agreement, providing visualization of agreement and identification of any concentration dependent trends relative to clinically relevant decision ranges.

Analytical precision was evaluated using a 15 × 2 × 3 design (15 days, two runs per day, three replicates per run) to estimate repeatability and within-laboratory precision.

Reproducibility was assessed using a 5 × 5 × 3 design (five days, five replicates per day, three instruments) to estimate between-site and total reproducibility. Testing included low, mid, and high Total T4 concentrations for both canine and feline lithium heparin plasma samples, representative of clinically relevant ranges.

Potential interference from common endogenous substances was evaluated following CLSI EPO7 principles. Interferents included protein, bilirubin, cholesterol, hemoglobin, and triglycerides tested at clinically relevant high concentrations.

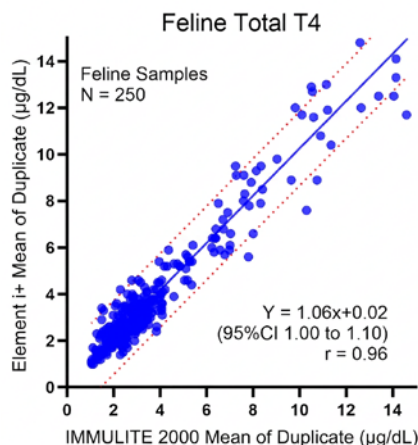
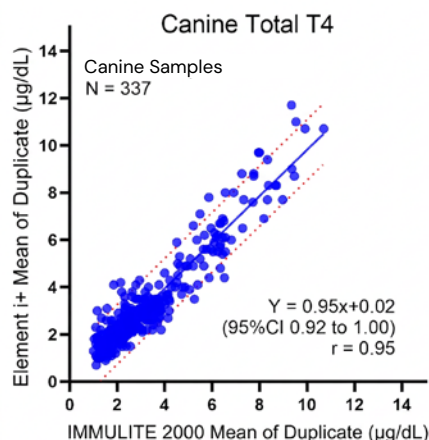
Cross reactivity was assessed with structurally related thyroid hormones, metabolites, and commonly co-administered compounds, including T3, iodothyronine derivatives, antithyroid agents, and selected pharmaceuticals, tested at supratherapeutic concentrations.

Results

Method comparison regression plot analysis, which was based on the mean of duplicate results, demonstrated excellent agreement with the reference method (canine slope ≈ 0.95, feline slope ≈ 1.06). The method meets the acceptance criterion for proportional bias. The regression analysis for samples (1–15 µg/dL) yielded a slope with a 95% confidence interval that is fully contained within the required 20% range.

The Bland–Altman analysis, using a single replicate on both platforms, shows a mean bias for canines 0.11 µg/dL (1.4 nmol/L) and for felines –0.07 µg/dL (–0.9 nmol/L) for samples in the reportable range.

Regression Plots



Precision: Study demonstrated CVs $\leq 15\%$ for 1–20 µg/dL (13–257 nmol/L)

Reproducibility: Study demonstrated CVs $\leq 16\%$ for 1–20 µg/dL (13–257 nmol/L)

Interference: No clinically significant effect from protein (8 g/dL), bilirubin (35 mg/dL), cholesterol (600 mg/dL), hemoglobin (1,000 mg/dL), or triglycerides (1,000 mg/dL)

Cross Reactivity: Minimal analytical cross reactivity was observed with structurally related thyroid hormones, iodothyronine derivatives, antithyroid agents, and commonly co-administered pharmaceuticals, with all tested substances producing $\leq 1\%$ change in measured Total T4 concentrations. An exception was tetraiodothyroacetic acid, which demonstrated 7% cross-reactivity at a concentration of 10 µg/dL and should have minimal expected impact on routine clinical testing.

Conclusion

The Element i+ Total T4 assay provides accurate, precise, and reliable in-hospital thyroid testing aligned with reference-laboratory methods, supporting confident diagnosis and monitoring of thyroid disease in dogs and cats.