of the expected values for all the immunoassay techniques; HPLC assays gave results -6.5% below the expected values. However, last year, nine blood samples supplemented with cyclosporin to concentrations in the range 50-1100 µg/L were circulated as part of the UK Quality Assessment Scheme. The results for the analysis of these samples are summarized in Figure 1. The median deviation from the target values was -2%, +3%, and 0% for the EMIT assay (Syva, San Jose, CA), the HPLC assays, and the TDX monoclonal assay (Abbott Laboratories, Chicago, IL), respectively, but was +13% for the CYCLO-Trac SP assay. The percentage bias was positive over the concentration range, and the degree of bias was not related to the concentration measured.

The mean result for a blood sample circulated by the UK scheme in March 1993, with a nominal cyclosporine concentration of 500 µg/L, was significantly higher by the CYCLO-Trac SP than the three other methods (P <0.001, one-way ANOVA). The mean results (and number of centers reporting) were: 528 (7), 549 (79), 504 (20), and 617 (69) µg/L for HPLC, TDX, EMIT, and CYCLO-Trac SP assays, respectively. A frequency histogram of the CYCLO-Trac SP results for this sample made apparent a bimodal distribution of results, with modes of -525 and -645 µg/L. This distribution may be the result of the use of in-house calibrators by some centers, rather than those supplied with the kit, so that some values were closer to the nominal weighed-in concentration (500 µg/L). For instance, the result for this sample reported by our laboratory, using in-house calibrators prepared independently of the UK Cyclo-

sporin Quality Assessment Scheme samples, was 531 µg/L.

These findings have prompted us to reexamine the issue of calibration of the CYCLO-Trac SP assay, and we intend to revert to the practice of asking participants who are using this assay to indicate the source of their calibrators (2). By recording this information, we should be able to determine whether the change in the relative performance of this assay can be attributed solely to between-method differences in calibration.

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References

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An investigator for the manufacturer comments:

To the Editor:

Little is known about the factors that influence thiourea metabolism and excretion in humans. Concentrations in urine are greatly increased in sulfituria oxidase deficiency (1), and colonic bacteria may have a role in the formation of urinary thiourea (2, 3). Thiourea is an intermediate metabolism in the oxidation of reduced sulfur products of bacterial metabolism (e.g., hydrogen sulfide). Endogenous pathways for the formation of thiourea have also been suggested (4).

We have developed a sensitive, simple colorimetric method based on a previously described ferric nitrate reaction (5, 6); the method is suitable for investigating some of the factors that influence thiourea excretion in humans. To remove endogenous interfering factors from urine, we use a Sep-Pak C\(_{18}\) cartridge (Waters, Milford, MA), washed consecutively with 2 mL of methanol and 4 mL of 10 mmol/L NaOH before use. Urine (10 mL) was adjusted to about pH 9.0 with 50 µL of 10 mol/L NaOH and centrifuged at 3000 x g for 10 min to remove particulate matter. Aliquots (2.2 mL) of supernate were passed through individual Sep-Pak C\(_{18}\) cartridges, and washed through with 1.0

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Improved Colorimetric Determination of Urinary Thiourea to Study Intermediate Sulfur Metabolism in Humans

To the Editor:

Little is known about the factors that influence thiourea metabolism and excretion in humans. Concentrations in urine are greatly increased in sulfituria oxidase deficiency (1), and colonic bacteria may have a role in the formation of urinary thiourea (2, 3). Thiourea is an intermediate metabolism in the oxidation of reduced sulfur products of bacterial metabolism (e.g., hydrogen sulfide). Endogenous pathways for the formation of thiourea have also been suggested (4).

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