with therapeutic response. P-gp is involved in the disposition and uptake of several antidepressants into the brain, including amitriptyline and its primary metabolite, nortriptyline. However, these effects appear to be of minor clinical significance compared with CYP2D6 and CYP2C19 sequence variations that alter drug metabolism in vivo.

References
9. Kushler and Hurley (7) tested Bissell’s method and concluded that it is easy computed and gives reasonably accurate results.
10. Taking into account the mathematical equivalence of ΔSE_c, ΔREC, and Cpk, it is possible to find approximate two-sided CIs for ΔSE_c and ΔREC. By rearranging Eqs. 4 and 5, we can derive the confidence interval for ΔSE_c:

\[
ΔSE_c = z_2 \sqrt{\frac{1}{n} + \frac{C_{pk}^2}{2n - 2}}
\]

and the confidence interval for ΔREC:

\[
ΔRE_c = z_2 \sqrt{\frac{1}{n} + \frac{ΔREC^2}{2n - 2}}
\]

CIs calculated for critical errors depend on the number of measurement results used in calculating them. Decisions on the adequacy of quality-control algorithms may be highly uncertain when based on a small number of measurement results. Such a situation might occur in a medical laboratory; for example, when a measurement method is newly introduced into routine practice. A minimum of 20 results is typically used to form an initial esti-
mation of the measurement’s performance (8). These 20 results are, however, insufficient for reliable quality-control planning. Further updating of the initial estimation as new results are obtained is obligatory.

Through the calculation of CIs for critical errors with the above formulas, it is possible to quantify the reliability of quality judgments. This analysis highlights the significant variability that may exist in such judgments because of the random nature and limited quantity of quality control data. Caution should be exercised when interpreting such data and making decisions on an appropriate quality-control strategy.

References


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Characterization of Interference with 6 Commercial Δ²-Tetrahydrocannabinol Immunoassays by Efavirenz (Glucuronide) in Urine

To the Editor:

We observed that antiretroviral therapy with efavirenz (EFV) produces urine samples that screen positive for Δ²-tetrahydrocannabinol (THC) exposure, despite the absence of 11-nor-Δ²-tetrahydrocannabinol-9-carboxylic acid (THC metabolite). These observations were made when we were using immunoassay-based reagents to screen for drugs of abuse in patients enrolled in a study on the effects of inhaled marijuana on HIV-related neuropa-thy. Extensive anecdotal literature exists regarding the interference of EFV with antibody-based assays for THC metabolites in urine. In product literature, the manufacturer of EFV (Sustiva®; BMS Virology) states that EFV may interfere with THC metabolite immunoassays (1). An earlier letter to Clinical Chemistry discusses the interference of EFV with an ELISA for estradiol (2). We therefore characterized the occurrence of EFV cross-reactivity with several commercial reagents used to screen for THC exposure.

We hypothesized that cross-reactivity with THC immunoassays was the result of the interaction of EFV metabolite (and not a parent drug) with the antibody complexes used in the assays. The majority of EFV in urine exists as an 8-position hydroxylated metabolite [8-hydroxy-efavirenz (EFV-8-OH)] and/or its 8-ether glucuronide (EFV-8-G) (3). Findings with 2 different THC immunoassays [Instant-View MultiDrug Screen Urine Test (Alfa Scientific Designs, Inc.) and Cannabinoids (THCA/C/THC) Direct ELISA Kit (Immunalysis Corporation)] revealed that cross-reactivity was attributable to EFV-8-G, and not EFV-8-OH or a parent drug. Initial studies were performed after isolation of the parent drug and metabolites from EFV tablets by organic solvent extraction and from EFV-positive urine by HPLC fraction collection, respectively. Naive urine was then supplemented with EFV-8-OH, EFV, or E-8-G. Urine containing EFV-8-OH or EFV alone exhibited negligible and no cross-reactivity, respectively, whereas naive urine supplemented with EFV-8-G exhibited a threshold-bound, concentration-independent cross-reactivity similar to that observed in urine from patients undergoing EFV therapy. Furthermore, hydrolysis of EFV-positive urine by either enzymatic (glucuronidase) or acidic thermal treatment abolished the interference. These initial observations support the hypothesis that EFV interference with THC immunoassays is mediated through cross-reactivity involving EFV-8-G, supporting the need to characterize the EFV-related interference with THC immunoassays.

Urine from 8 individuals undergoing antiretroviral therapy with 600 mg EFV/day were randomized for analysis by 6 different instrument-based THC immunoassays. Patients providing urine for these studies gave informed consent before analyses, and the studies were performed in accordance with guidelines established by the University of California, San Diego, Institutional Review Board and Human Subjects Committee. Hydrolyzed duplicates of each sample were also prepared by the addition of 50 µL of concentrated HCl/mL of urine, followed by heating to 80 °C in a laboratory microwave oven (20 s at a relative power setting of high). Concentrations of EFV, EFV-8-OH, and EFV-8-G were determined by HPLC with ultraviolet detection. The purity and identity of each HPLC peak were confirmed by nanospray tandem mass spectrometry (MS/MS) (4). Table 1 presents data for the above concentrations and the responses of 6 commercial THC immunoassays to urine from patients undergoing EFV therapy. These data show that immunoassays performed with reagents from Microgenics Corporation (Cedia® Dau MultiLevel THC), BioSite Incorporated (Triage® TOX Drug Screen), and Im-