Reviewer's report

Title: Challenges and limitations of routine immunoassay-based drug of abuse/toxicology screening used in emergency medicine

Version: 1 Date: 24 March 2009

Reviewer: Jeffrey Brent

Reviewer's report:

You have provided an analysis of the state-of-the-art regarding cross reactivity in drug abuse and toxicology screening. As part of your analysis you used molecular similarity analysis to explain the observed false-negatives and cross reactions. You further investigated the causes for cross reactions seen in PCP and TCA immunoassays.

In providing this information you have also given us a comprehensive treatise on many aspects of the screening immunoassays.

In your analysis of PCP-positive screens you have found, although with a small sample of only 10 patients, what most people around the country have been also noting – that most PCP positives on immuno assays are actually false-positives. Similarly, you point out, which I think is also commonly observed, that the most common reason for positive PCP assays is cross reactivity with dextromethorphan.

Your studies on TCA assays point out that the most common cross reactor is cyclobenzaprine. As you point out, there is considerable use of this agent in contemporary medical practice. Your integration of market usage is a nice addition to this paper.

Given that these immunoassays have been around for many years, it is clear from the data that you present that many of them are out of date and do not reflect current patterns of either illicit or therapeutic drug usage.

The supplemental material serves as a good reference.

For the clinician, the explanation about why we have these false-negatives and false-positives is not immediately applicable clinically. However, being aware of these common pitfalls in the interpretation of screening immunoassays is of considerable importance. Please note that reference 3 on page 5 only deals with drug-drug interactions and not the other issues which are described in that sentence.