Reviewer’s report

Title: Accidental intoxications in toddlers: lack of cross-reactivity of vilazodone and its urinary metabolite M17 with drug of abuse screening immunoassays

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Reviewer: Christine Lh Snozek

Reviewer’s report:

The authors present a study evaluating vilazodone and its metabolite for cross-reactivity in an amphetamines immunoassay. The manuscript is well-written and easily understood. Some suggestions for improvement are included below:

The title is somewhat misleading, as it implies that cross-reactivity was noted. Would revise to more clearly reflect the results of the study.

Abstract stated vilazodone & metabolite 'did not cross react on any immunoassays', which implies that multiple amphetamines immunoassays were evaluated whereas only the Roche cobas methods were tested. Given that the patient reports were only of false-positive amphetamines screens & the low predicted cross-reactivity with any of the other DOA tests included in the study, it makes more sense for the abstract to refer specifically to the one method tested.

Line 109, "hydroxy" is missing the r

The authors might add a few comments to describe why 2D modeling is adequate, when antibodies recognize 3D structures.

Line 261 the word screening is duplicated

The discussion of haptens in the methods largely duplicates what's in the discussion section. Would keep in only one location; could probably remove from methods

Lines 296-298, the sentence is awkward. "immunoassays" should be plural or the sentence should refer more specifically to a single immunoassay. Similar issue with lines 316-318

Since vilazodone is commercially available and showed predicted cross-reactivity with TCA immunoassays, it would be interesting & provide additional support for the model's predictive capacity if the drug were tested on TCA screens. Possibly could be its own publication, since it's a bit of a tangent from amphetamines.

Would strengthen the study to test the metabolite on other amphetamines immunoassay platforms as well, since each uses distinct antibodies for recognition.
Have the authors investigated adult urine samples for false-positive results? Would strengthen the conclusion that the responsible factor was a childhood-specific metabolite if urine from adult overdoses did not provide positive results.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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