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

Version: 0 Date: 16 Sep 2018

Reviewer: Isabel Gomila

Reviewer’s report:

In this manuscript the authors investigated drug of abuse immunoassay cross-reactivity of vilazodone and metabolites using computational and empirical approaches. The starting point of the work were two cases of accidental vilazodone exposure in toddlers with unexplained positive amphetamine urine immunoassay drug screens. However, some aspects should be reviewed:

1. In my opinion, the work should focus on the possible cross-reactivity of vilazodone in amphetamine immunoassays, since no date of suspected cross-reactivity with other immunoassays (cannabis, cocaine, barbiturates, ...) is reported.

2. The case reports of vilazodone exposure on which this study is based should be described in the article, since the information available in the references provided is very scarce.

3. Results of amphetamine immunoassays were reported in case report of vilazodone ingestions in young children cited in the manuscript?

4. Cross-reactivity testing was performed up to a concentration of 100,000 ng/mL. What levels of vilazodone or its metabolites could be expected in the urine in cases of overdose?

5. In discussion, the authors state "The similarity of vilazodone overdoses to amphetamines toxicity demonstrate the importance of confirmatory analysis to rule out amphetamine and methamphetamine exposure”. However, the study seems to rule out that positive amphetamine results were caused by vilazodone. Could you explain this point?

6. An important limitation of the study is the lack of confirmation of positive amphetamine results by a reference method, such as GC-MS or LC-MS/MS. These methods would have allowed excluding causes of false positive other than viladozone.

7. Table 1 does not provide additional information to the text and could be eliminated.

8. The description of Chemical Synthesis of Vilazodone Metabolite M17 should be summarized.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
No

**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.

No

**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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