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Name of Journal: *World Journal of Clinical Pediatrics*

ESPS Manuscript NO: 21763

Manuscript Type: REVIEW

November 14, 2015

Mr Shui Qiu
Science Editor, Editorial Office
Baishideng Publishing Group Inc
World Journal of Clinical Pediatrics

RE: Synthetic Cannabinoids 2015: An update for pediatricians in clinical practice

Dear Mr Qui:

Please find attached our revised manuscript, entitled "*Synthetic Cannabinoids 2015: An update for pediatricians in clinical practice*," which you have allowed us to revise for publication in the *World Journal of Clinical Pediatrics*.

We have revised the manuscript and included the required documents. We have submitted the signed Conflict of Interest and Copyright Assignment forms as well as the Audio Core Tip file. All of the references have been rechecked and updated with the PubMed and DOI numbers verified.

We were pleased that you and the reviewers found merits in the manuscript. We believe the points raised by the reviewers were constructive and that thoughtful consideration of each has resulted in an improved manuscript. You will find that each of their concerns and comments have been addressed. Sections of the manuscript that have been modified as a response to the reviewer comments remain highlighted in red. We have included all of the reviewers' comments in this letter (in italics) followed by our response to each comment.

Reviewer 1

The Reviewer wrote:

Well written and designed study. Most practitioners are mostly unaware of the staggering speed by which drugs are modifying and released in the street. This review gives pediatricians, ER doctors and physicians at large a view of what they are facing and the important message is that a negative urine screen does not rule out SC intoxication. This is especially true in a busy ER screening so that physicians should not think about other DDs for their patient's clinical picture. I think this is an important message to be conveyed in the conclusion.

We appreciate the reviewer's feedback on this important issue. No changes were recommended by Reviewer 1.

Reviewer 2

Reviewer 2 made several specific suggestions. The Reviewer wrote:

1. *Introduction// Please include comment about current estimates indicate young secondary school students in the United States (8th grade) are using SC more than older students, including those in college (para two.)*
We have addressed this issue on page 6 – “The rise in use of SCs among younger individuals is particularly alarming. Among 8th graders SCs are the third highest category of illicit drug being used after marijuana and inhalants^[9].”
2. *Clinical effects//Consider using dysrhythmia instead of arrhythmia (para 4).*
We have changed the term to dysrhythmia (page 12).
3. *Evaluation// Consider including an estimate of the number of adolescents using SCs and other substances, such as ethanol. (para 3).*
This issue is addressed on page 17 - “Alcohol and drug use are not rare in teenagers. Seventy percent of 12th graders in the US are reported to have at least tried alcohol. Marijuana is by far the most widely used illicit drug used by youth in the US. The most commonly used illicit drugs by 12th graders (lifetime) include marijuana (45%), ecstasy (7.2%) and cocaine (4.9)^[9].”
4. *Treatment// Please provide guidelines for the inpatient vs outpatient treatment of these patients because SCs appear to have more psychological effects than marijuana.*
This issue is addressed on page 21 – “Synthetic cannabinoids can be more psychologically addictive than marijuana. Outpatient services are a viable option for less severe cases, especially if synthetic cannabinoids are the only drugs being used and the youngster is displaying little or no symptoms of withdrawal. Inpatient or residential treatment centers offer intensive care that can help youth get through the early stages of withdrawal in a prompt manner. The length of inpatient or residential synthetic cannabinoids treatment depends on the severity of the use and/or addiction, whether the youngster is also abusing other substances and varies from patient to patient.”

In summary, we again thank you and the reviewers for thoughtful and constructive comments. We have attempted to address them thoroughly, and we believe that the manuscript is improved for it. We remain confident that it will be a timely, informative and useful contribution to the literature, and of interest to the readership of the *World Journal of Clinical Pediatrics*. As before, the manuscript has not been published elsewhere, is not being reviewed for publication by any other journals and no potential conflicts of interest exist on the part of the authors.

I hope that you find the revised manuscript acceptable for publication in the *World Journal of Clinical Pediatrics*. Please let us know if there are any other questions. Thank you.

Sincerely,

Name: Daniel Castellanos

Signature: 

Date: 11.09.15

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