

Peer Review

Review of: "Exposure to Benzene, Toluene, and Xylenes from Electronic Cigarette Use Compared to Working Environment Permissible Exposure Limits: A Risk Assessment Analysis of a Recent Publication"

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This investigation into the toxic potential of exposure to Benzene, Toluene, and Xylenes (BTX) via electronic cigarettes is mostly intended to provide some corrections to a prior publication as well as to move the science forward systematically. The paper does well to explain the background, their (more appropriate) methods, and the presentation of their results. This is especially true where they believe that there were issues with the initial methodology and the likely erroneous conclusions that could be drawn from these results. Overall, this investigation and associated paper will add to the growing body of nuanced findings related to electronic cigarette use/vaping, VOCs, and health outcomes. I do suggest a few minor revisions to improve this manuscript. Please see specific suggestions below.

- The use of the phrase “electronic cigarette (or e-cigarette)” is good and applicable, but authors might benefit from including “vaping” earlier in the manuscript, as this term is also associated, and the authors use this in multiple places throughout the manuscript. This, however, also needs to be distinguished from the inhalation of cannabis vapor or cannabinoids using similar electronic vaporization methods, as the “juice” comprising each of these is distinctly unique even given the shared method of use.
- The authors in the current investigation state that the prior investigation was done utilizing “illegal disposable vaping devices.” However, this is a little at odds with the title of the original

article, which stated that these were “commercially available.” It appears that there is a shifting landscape that has been moving for a while, with some of this being a presidential decree in 2022 and then movement more recently as a constitutional reform as of Dec 2024. Perhaps a brief discussion in the introduction about their legal status in Mexico, as well as their continued use despite these constraints, is warranted.

- Also needing to be included in this is that when something becomes illegal where the desire for products remains, the illicit market will rise up to meet the need. This product, however, will be devoid of regulations and other components that provide minimum health and safety standards. This could lead to impacts on the nicotine liquid itself and likely the electronic components that would make some of the assumptions (e.g., sub 300-degree temperatures) a little dubious. Some speculation on the differences between the legal and regulated vs. the illicit market is warranted, as this could impact levels found.
- This may be more so with cannabis vapor liquid, but what is the extraction method used for nicotine salt? If it is a solvent extraction method that is done poorly or hurriedly, some of the solvents used may remain within extracted components, especially if under seal, as is done with electronic vape cartridges, especially in disposables. Perhaps this can be included as a point of distinction or as a shared issue between nicotine vs. cannabis vapes if the authors choose to address some of the previous comments.
- Within the methods section, there is a sentence, “For benzene we used the formula (molecular weight: 78.11) to calculate” however, this sentence reads poorly and initially indicates that the weight *is the formula* used or that this formula was used differently for benzene than the others. Please adjust this so that it conveys the intention of the authors more clearly.
- The sentence, “In reality, and based on an average.....” is slightly repetitious of sentiments in the introduction and seems misplaced within the methods section of the current paper. While this may have been the impetus for your manuscript, it isn’t a part of your methods and may confuse the reader. The sentence, “in this study, we performed a more appropriate.....” is sufficient, serves a similar purpose, and fits well within the methods while reminding the reader of why you are performing this analysis.
- Authors state that they assumed “a 5 mL per day average liquid consumption for vaping” and earlier they state that this was from a survey. If this is from another article that conducted a survey, state the article; if this was the authors' own unpublished survey, then that should also be

stated. Basically, authors should clearly cite where the information that is the basis for the assumption can be found or requested.

- The authors provide a PEL to Aerosol ratio within their table. It is unclear what the benefit of this ratio would be, except to try to demonstrate how “wrong” the previous publication was when reporting or interpreting their values in comparison to the PELs. A comparison of the aerosol column with the PEL exposure column would sufficiently demonstrate that none of the values are anywhere close to the PEL. A specific rationale for the presentation of this ratio would clarify this to the reader. If there is a more practical application for presenting the data in this fashion, it should be clearly stated. I do not think that the ratio is needed given the solid foundation and arguments about the calculations that the prior and current investigations utilized, as well as the remaining parts of the table besides the ratio. Providing the “x-fold lower” values within the text of the results does, however, seem warranted.
- There are some issues with the presentation of results. For example, “EC use would expose users to 865 to 15,990-fold lower levels of benzene compared to working for 8 hours in an environment with benzene levels at the PEL, more than 3 to 4 orders of magnitude difference.” is confusing. How are the authors considering magnitudes of difference, and how is 865 at the lowest end only 3 to 4 orders of magnitude different? and different from what? What comparison is being made with these results here? I am sure that the authors know what comparisons as well as the point they are making; however, its conveyance to the reader isn’t as clear as the authors intend.
- The authors make an exceptional point when discussing the challenge with toxicological comparisons and the inclusion of exposure time as a variable. This point is well heard and is really the crux of the argument against the previous publication. This should be stated in the introduction as clearly as it is here in the discussion.
- The authors do make a good case in the discussion that the level of these compounds is expected to be low and state a few previous studies that support this view. That said, I do think that they need to include a few caveats. First, the proper functioning of the electronics would keep the temperature below 300 degrees, but this may not be true for all units or those with damage (e.g., manufacturing defects, drop damage, user tampering, etc....). Additionally, usage patterns such as inhaling for longer or more puffs in quick succession may lead to increased heat and potential production. Secondly, these were tested in new cartridges and may not accurately demonstrate the concentrations that may be seen at the end when someone is trying to get their money’s worth, as

it were, and continuing to use with low solution volume, causing more than just VOCs, potentially including filament particulate and metal contaminants to be consumed.

- The authors' conjecture of the results being related to "background air, analytical equipment, or laboratory reagents" is speculative at best. The current authors do back this up with the context that the previous authors didn't use a "true control" and other investigations have failed to find similar values; however, the speculation that these values would be found due to "background air" is not as likely as the issue of damaged or malfunctioning analytical equipment or less potent/old laboratory reagents. The authors should attempt to provide this context. Additionally, VOCs, including BTX, can be found proximally to newly created plastics, and since these were specifically new e-cigarettes, one cannot negate the issue of the VOCs from the plastics comprising the e-cigarette as well (albeit this would still not account for the levels that were found by the original authors).
- Suggest to include authors in the statement, "...contains so many errors, including errors in converting between different units (ppm to ug/L), that authors and editors should consider the possibility of retraction." It is likely that the authors themselves would want to have this addressed once all of the issues with their prior publication are stated and they find them to be well-founded and demonstrated.

Declarations

Potential competing interests: No potential competing interests to declare.