

Author's response to reviews

Title: Biological Exposure Assessment to Tetrachloroethylene for Workers in the Dry Cleaning Industry

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Author's response to reviews: see over

Editor-in-Chief
Environmental Health

Dear Editor:

On behalf of my co-authors, I am submitting the revised manuscript “Biological Exposure Assessment to Tetrachloroethylene for Workers in the Dry Cleaning Industry” for consideration for publication in Environmental Health.

The manuscript has been modified to address the issues raised by the reviewers.

Dr. Kirkleit’s comments:

General

The manuscript would benefit from a better discussion and interpretation of the results in the present study, including reported exposure levels, temporal variation in the concentration of PCE and trichloroacetic acid (TCA) in biological media as well as correlations between the various exposure indices, in respect to both existing recommendations on biomonitoring of PCE (ACGIH and Deutsche Forschungsgemeinschaft (DFG)) and findings from other studies comparing various exposure indices of PCE (Gobba et al. 2003;Furuki et al. 2000;Lauwerys et al. 1983).

Our response

We have expanded the background to include more exposure limits and recommendations, expanded the discussion to include comparison with other biomonitoring studies of PCE, and discussed why we did not strictly follow the ACGIH guidelines.

1. What is the aim of the study? The conclusion does not match the aim of the study stated as “to assess the feasibility of a comprehensive PCE exposure assessment for employees working in the dry cleaning industry”. Further, it is not clear what the main objective of the study is. Is it to assess the feasibility of a comprehensive PCE exposure assessment for employees working in the dry cleaning industry in general (Abstract, Method section page 5), or did the author want to focus on women’s exposure to PCE due to a higher amount of adipose tissue (Introduction section page 5).

Our response

We have expanded the introduction to include more information about the larger pilot biomarker study of which this exposure assessment was a part. Some of the study parameters (e.g. restricting the study to women participants) were due to the focus of the larger pilot biomarker study. The aim and conclusion have been modified as well.

2. Study population As discussed in the manuscript (Introduction, Limitations of study, page 17) the participating facilities were self-selected. What does this mean? A better description of the selection criteria and the study population must be given. It seems from the discussion that the study aimed at a larger number of dry cleaning shops and workers than included. How many workers did the study aim at? On what basis were the four dry cleaning shops selected from the originally 175 dry cleaning shops? Why were only 3 operators (one full time and two part-time), the job category assumed to have the highest exposure, included? Does smoking affect the level of biomarkers for PCE exposure? If so, a discussion of this should be given in the discussion section and the information on smoking habits provided by the participants should be used in the analysis or interpretation of the results. If not this information should be removed. Except from number of years employed in the dry cleaning industry, the information on work history is not used in the study. The information on height and weight given by the participants are not used in the analysis (the physicians measurements are) and should be removed from the manuscript.

Our response

The introduction now includes more information on shop recruitment and selection. Because women are less likely than men to be operators, we found only three full- or part-time operators in our study population.

Smoking data were collected because several of the biomarkers of effect we studied are affected by cigarette smoke as well as by workplace chemicals. In addition, we assumed that smokers would have more contaminated-hand-to-mouth contact than nonsmokers and thus might have higher biological levels of PCE or its metabolites. However, a re-analysis of the biological levels comparing smokers and nonsmokers found no difference, so we removed the smoking data from the table as not pertinent to this paper.

As all the dry cleaners were measured and weighed during physician visits, we have also removed the self-reported height and weight.

3. Sampling protocol i) As the authors conclude, the sampling strategy was challenging to implement due to frequent last minute changes to work schedule and collection of multiple samples. It is not clear whether these logistic constraints posed limitations on the sampling protocol in a negative way. Information on this will make the manuscript more transparent.

Our response

More information about how the flexible work schedules conflicted with the sampling protocol has been added to the discussion.

ii) What was the rationale behind the sampling protocol? In the introduction the authors refers to the guidelines given by ACGIH on how to assess workers' exposure to PCE.

The ACGIH (2000) recommends that for PCE the sampling time should be prior to last shift of workweek for both PCE in end-exhaled air and blood, while trichloroacetic acid (TCA) in urine should be sampled end of shift at end of workweek. If the purpose was to assess the feasibility of a comprehensive PCE exposure assessment for these employees, as stated in the method section (first paragraph), why wasn't the recommendations from ACGIH implemented into the sampling protocol? That is; why was only a single measurement of PCE in blood included, and why was the blood sample prior to the last shift of work week (Friday) excluded? The rationale for the study protocol should anyhow be given. It would be useful for the readers if this was discussed in relation to the toxicokinetics of PCE either in the introduction section or discussion section of the article.

Our response

Conducting a study in a number of small retail establishments with a few workers each differs markedly from conducting a study in a large factory. Where there are only a few workers, days and hours of work tend to vary from worker to worker and from week to week. Because most shops are open on Saturdays, some workers choose to or are asked to work that day, taking another day (often, Friday) off instead.

Blood collection was done on Thursday as we had observed, in other studies of dry cleaners and in work done in preparation for this study, that attendance on Fridays was spotty and those working on Friday usually left early. For these reason we did not strictly follow the ACGIH recommendations.

Our colleagues at NCEH have determined that one blood specimen is sufficient to measure occupational and environmental contaminants. We think that asking for a second blood specimen would have reduced our participation rate—as it was some potential participants declined to participate because of the blood draw.

Much of the above has been added to the discussion.

iii) The sampling protocol in table 1 is difficult to understand. A description of the purpose of the different subsets, together with the number of included workers, should be given in the table. The protocol for all the participants (n=18) and the protocol for the subgroup (n=13) should be separated in the table. Further, the reason for excluding 5 workers in week 2-5 should also be given.

Our response

The five workers not included in the weekend measurements were excluded for a logistic reason—the distance of their facility from our laboratories. This information has been added to the table and the core sampling and elimination sampling have been separated.

iv) According to the Health & Safety Laboratory (2002) TCA in urine is unlikely to be a suitable biological indicator of PCE-uptake due to the small percentage of solvent excreted in urine. This has also been reported in other studies. Why was this marker one of the major biomarkers utilized in the present study?

Our response

The larger PCE biomarker study includes components such as physiologically based pharmacokinetic modeling tracking both the major and minor PCE metabolites, measurement of kidney proteins excreted in the urine, and measurement of markers of oxidative damage to DNA. For this reason we asked participants to collect urine specimens.

v) The general population might be exposed to PCE through ground water, drinking water and food (IARC, 1995). Since the study did not include a reference group assumed not to be occupationally exposed to PCE, why did not the sampling protocol include baseline measurements for the participants?

Our response

The study did include a reference group (laundry workers). As we reported previously (Toraason et al 2003) their PCE blood levels were two orders of magnitude lower than those of the dry cleaners. This information and the Toraason reference have been added to the manuscript.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Introduction

i) The ethical considerations and approvals in the introduction (page 5) should be placed in the Method section.

Our response

Done

ii) IARC (1995) has classified TCE as a group 2A carcinogen (probably carcinogenic to humans), while occupational exposures in dry cleaning is grouped as 2B (possibly carcinogenic to humans). The sentence must be rephrased accordingly.

Our response

Done

2. Method

Please give the temperature during storage and transportation for both personal sampling of ambient air, blood samples and urine samples. Was the temperature at the time of sampling the exhaled air logged?

Our response

We have changed the Methods section to indicate the general temperatures at which specimens were collected, transported, stored, and analyzed, and made the wording more clear.

Temperatures at the times of sampling the exhaled air were not logged. However the times were, and official temperatures are available. During the data-collection period from July 30, 1998, to December 9, 1998, mean temperatures ranged from 2 to 27° C and from a minimum of -4° C to a maximum of 36° C. Many specimens were collected in the early morning (5-6 am) or in the early afternoon, so a wide range of ambient temperatures was experienced.

Our protocol stated that breath samples that had cooled would be reheated to 37° C. before injection into the gas chromatograph. In practice, samples that had cooled were allowed to come to ambient room temperature (~23° C.) before injection.

3. Results i) The arithmetic mean and range of the various exposure indices should be given in addition to geometric mean.

Our response

We have added these.

ii) The abbreviations AM and PM in table 1 are not given in the table nor in the text.

Our response

Table 1 is now footnoted to explain AM and PM.

References

Furuki K et al. Monitoring of occupational exposure to tetrachloroethylene by analysis for unmetabolized tetrachloroethene in blood and urine in comparison with urinalysis for trichloroacetic acid. *Int Arch Occup Environ Health*. 2000;73:221-227.

Gobba F et al. Perchloroethylene in alveolar air, blood, and urine as biologic indices of low-level exposure. J Occup Occup Environ Med. 2003;45(11):1152-1157.

Health and Safety Laboratory. Guidance on laboratory techniques in occupational medicine. Ninth edition, 2002.

IARC. Volume 63, 1995. Available at <http://monographs.iarc.fr/ENG/Classification/Listagentsalphorder.pdf>

Lauwerys R et al. Health surveillance of workers exposed to tetrachloroethylene in dry-cleaning shops. In Arch Occup Environ Health. 1983;52:69-77.

Our response

All of these except for the Gobba and the Health and Safety Laboratory (HSL) references were already cited. We have added the Gobba reference. Trying to locate the document I wrote to HSL and received the following response:

From: Sharon.Taylor@hsl.gov.uk [mailto:Sharon.Taylor@hsl.gov.uk] **On Behalf Of** HSLINFO@hsl.gov.uk
Sent: Thursday, January 17, 2008 4:20 AM
To: Ruder, Avima M. (CDC/NIOSH/DSHEFS)
Subject: Re: Guidance on Laboratory Techniques in Occupational Medicine, 9th edition, 2002

Unfortunately this is an internal report only available to staff.

Therefore we cannot obtain and so will not cite this report.

Dr. Gobba's comments:

The study is certainly interesting, and well performed. I agree partly on the conclusions, but I have some observations.

Major Observations

All examined workers were women: gender related differences in PCE toxicokinetics are likely, as recognised by the Authors (MS, page 5).

Exposure in the examined group of workers was low compared to the current TLV proposed by ACGIH (about the 6%), and lower compared to other similar studies previously published in the scientific literature.

This is due to different reasons:

- in all the examined dry-cleaning shops, dry-cleaning machines contained refrigerated condensers, and 3 out of 4 also carbon adsorbers;
- 15 out of the 18 workers were pressers, not directly engaged in cleaning, while other 2 participants were part-time operators; only one worker was directly exposed to PCE

during loading and unloading of garments from the cleaning machines;

the Authors agree on the low exposure levels measured (page 18 of the MS).

Accordingly, the exposure levels observed in the study cannot be considered fully representative of the current exposure levels in the majority of dry-cleaning shops (at least considering Countries other than USA).

The low exposure levels are relevant in the results of biological monitoring as: -the body burden of PCE is low;

-at similar low levels, the correlation between PCE in air and urinary metabolites is usually low, while better correlations were reported between PCE in air and in breath, blood and urine (e.g. see Gobba et al, J Occup Environ Med 2003);

for these reasons, it is not surprising that, e.g. the declines in breath PCE from Friday to Monday are significant, while the declines in urinary TCA are not.

On my opinion the results of the study, in agreement with other studies, confirm :

1) that unmodified PCE in breath, blood and urine are good exposure indices for low level of PCE exposure in dry cleaning, while urinary metabolites are not;

2) that also at low exposure levels (e.g. about 6% of the current TLV TWA ACGIH) a significant body burden of the solvent can be observed, confirming the need to perform the biological monitoring during the last day of the working week, as suggested by the ACGIH.

Regarding the use of air PCE sampling, we agree that it is certainly a good exposure index, and that it is certainly useful in the evaluation of exposure in group of workers (even if the use of passive samplers should be also considered, as they are simpler to manage compared to personal pumps).

On the other hand, we do not agree that air sampling can be considered an "appropriate surrogate" for the "absorbed dose" of PCE, at least on an individual level: in an individual worker, factors other than the environmental level of PCE can significantly influence the absorbed dose of the solvent, including work-load, gender, body burden, co-exposures etc. Accordingly, at the same TWA environmental level of PCE, the absorbed dose can be different in different workers (as it was demonstrated for other similar solvents).

We are not confident that the models observed in this study (Table 6) can be easily extrapolated to other group of workers, e.g. having higher exposure levels, different work-load, different age, gender etc.

These points 'd be cited and commented in the MS

Major Compulsory Revisions (that the author must respond to before a decision on

-as repeated measures of environmental and biological PCE exposure indices are presented, Authors have to include the CV % of the analytical methods in the Methods section;

Our response

The precision (CV%) and accuracy of NIOSH Method 1003 and NIOSH Method 3704 have been added to the Methods.

-as blood and TWA outcomes were right skewed (as expected), Authors should explain why breath PCE apparently was not (page 10 of the MS);

Our response

We don't know why breath PCE was not skewed, but we can provide some information concerning why we chose not to do a log transformation. The distribution of preshift breath pce over the Wednesday - Friday data was slightly positively skewed. The distribution of the logs was moderately negatively skewed, i.e. taking logs made the situation worse. The residuals for the non-logged variable from some models that were run on all of the Wednesday - Friday data and also on all of the Friday - Monday data were nearly symmetrical. Thus logs were not taken.

The above has been added to the ms.

Minor Essential Revisions -I suggest to the Authors to prepare a Figure with the values of PCE in breath measured on Friday and Monday (Table 5 of the MS);

Our response

The figure is attached. We could substitute it for the table or include it in addition. However, to us, it does not seem to be more informative than the table. We checked to see if exposure levels and changes in women with three consecutive Friday-Monday measurements differed from those in women whose three Friday-Monday measurements were not done in consecutive weeks. There were no significant statistical differences between the two groups.

-apparently some useful reference is not included in the References section

Our response

We have added some references mentioned by Dr. Kirkeleit, as well as some additional references, and cited these in the introduction and/or discussion.

I hope that the re-evaluation process finds the manuscript acceptable for publication in Environmental Health.

Sincerely Yours,

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