

Author's response to reviews

Title: Characterization of exposures to cleaning products used for common cleaning tasks in hospitals -a pilot study

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Author's response to reviews: see over

Dear Editor of the Environmental Health Journal,

We have carefully analyzed reviewers' comments and criticism of the original manuscript and would like to thank them for their overall constructive criticism and thoughtful suggestions. Serious efforts have been made by our group to address all of them. The point to point responses to the individual reviewers' comments are included in the following document and our comments are highlighted in blue. We hope that our work has produced satisfying changes in the manuscript.

Sincerely (in behalf of all authors),

Anila Bello

Response to reviewers' comments on the manuscript with title "**Characterization of occupational exposures to cleaning products used for common cleaning tasks –a pilot study on hospital cleaners**". **A. Bello A, M Quinn, M. Perry and D. Milton.**

Reviewer 1: Elise Pechter

1. Conclusion statements are included beyond the scope of the presented data.

a (P3). The authors describe use of a validated system, cite articles regarding its use, but do not describe how to use the method, or how the method was applied to this task.

To address the reviewer's concern, in the revised version of the manuscript we have included a paragraph describing the DREAM method. The reader can refer to the original reference for further information on the DREAM method. The last paragraph in the methods section describes how we applied the DREAM for assessing the potential for dermal exposure to common cleaning tasks.

(a. continues) Information is not provided about the limitations of the DREAM method which does not appear to evaluate whether cleaning products are sprayed onto rags or directly onto surface (only described as sprayed directly onto the surface in Figure 1. Nor does it appear to draw lessons from applying the method.

Theoretically, the surface material is an important factor impacting chemical exposures from surface cleaning. The DREAM does not take into consideration the surface material. However, application of DREAM may find important differences for the "rug cleaning tasks" compared to surface floor cleaning. These differences can be related to the

changes on the “deposition” route of exposure. Because the chemical is absorbed by the rug, it is possible that intensity of deposition will differ compared to the floor cleaning. Rug cleaning was not identified in the workplaces that we visited. Our further field evaluations will include rug cleaning in the exposure assessment strategy.

The major lesson we learned was that DREAM method can be useful for classifying cleaning tasks in different exposure categories (this conclusion was previously included in the discussion section). However, by applying the DREAM method we were not able to identify the exposure differences between mirror, sink and toilet bowl cleaning. At the same time we could not find a major difference between two different types of floor cleaning. As a result, we can conclude that DREAM allows only categorization of tasks with wide exposure ranges. Further workplace application of DREAM is needed.

b. P5. The extent to which most of the cleaning chemicals may permeate the skin..... The only literature cites are 3 articles about glycol ethers.

The point we wanted to make here was: There is a need to evaluate the potential for dermal absorption and systemic toxicity from dermal exposures in the case of cleaning agents. For example glycol ethers, commonly used chemicals in cleaners, can be absorbed through the skin. Evaluation of other cleaning ingredients in relationship with skin absorption and systemic toxicity is critical to further study the health impacts associated with cleaning product use.

To address reviewer’s concern we have reformulated the sentences and added one reference that shows the relationship of dermal exposures and systemic toxicity in the case of isocyanates (see discussion section). To our best knowledge, no human exposure assessment studies have assessed dermal exposures from cleaning and the potential for systemic toxicity.

c. P6. The statement that hospitals are driven to clean and disinfect “by the need to protect workers from transmission of blood borne pathogens” is not correct and not supported by data or references. Hospitals are driven by the need to protect patients from infection –fecal oral and blood borne.

On the point that cleaning is done to prevent all types of infection transmission, not just that from blood: we agree that all types of infection transmission are of concern (e.g. from fecal, saliva exposures, in addition to blood) but the OSHA blood borne pathogen standard is a main reason for the increased workplace awareness. The OSHA blood borne pathogens standard is cited in the manuscript.

d. P.8 The authors conclude that the products investigated “are representative of the major products/ingredients used in Mass, “because the “variability of ingredients within product lines were greater than the between the same product produced by different manufacturers”. This does not justify the cleaning that the products reviewed in 6 hospitals are representative of all hospitals.

Agree. This study is a pilot study and not a large scale evaluation of the products used in Massachusetts' hospitals. Hospitals were selected as much as possible to be representative of different sizes and locations. At the end of the manuscript (the limitations of the study) we state: "The results of this work are based on a small number of products. While we selected only few representative hospitals and products, it is possible that other products/ ingredients are used elsewhere".

e. P9 An "ingredient was considered to be more hazardous" but the criteria blur potential to cause harm and potential to be exposed. Hazard must be defined carefully. If the term means the potential to be exposed, then the method of use should be included. If it includes the potential for absorption, then clothing and shoes should be mentioned. If it includes the potential for absorption, then clothing and shoes should be mentioned. Method of application is subsumed under task frequency on page 10, which is confusing. If the evaluation is about relative hazard, information should be included about the severity of outcome, strength of the sensitizing or irritating potential and other capacity to cause harm. P16 describes that the window/mirror/glass cleaning product is sprayed – but not whether the target of the spray is the rag or surface.

Because cleaning products contain many hazardous ingredients, it was important to identify the ingredients that are markers of exposure for the purpose of further exposure evaluation. The ingredients were selected by considering both a) the human health effects with respect to respiratory and dermal sensitization and irritation, and b) the potential for workplace exposures.

The first selection criterion considered selection of all frequently used ingredients concerning the degree of these exposures in the workplace. Then, among all frequently found ingredients, we selected potential sensitizers and irritants (criteria 2). To identify sensitizers and irritants, we conducted a review of the existing literature on *human* health effects of frequently used ingredients.

All known potential human sensitizers were selected and prioritized in the list; given the concern that sensitization may happen at very low concentrations.

In the case of irritant ingredients further selection (criteria 3-4) considered their *relative* potential for workplace exposures, which were considered directly related to the ingredient's product concentrations and its volatility (relative to other mixture ingredients).

This strategy allowed *selection of* ingredients that were further evaluated for inhalation and dermal exposure potential using the selected qualitative /semi-qualitative methods that take in consideration other exposure determinants in the workplace.

2. Cleaning is not distinguished from disinfection, which is a key issue in hospitals.

a. Most of the literature cited is from domestic and commercial cleaning, with exception of reference 11, without comment about the absence of research on cleaning in health care settings (pp 3-4).

We have completely revised the background section. The new section is clearly showing the purpose of this exposure assessment study and addresses the need for research on hospital cleaners. Our study focuses on cleaning, however, the products themselves blur the distinction between cleaning and disinfecting because many products used primarily for cleaning have added a disinfecting agent to the ingredients. Some products are now advertised as a “cleaning and disinfecting solution.” In practice, some cleaners are using cleaning products because they think they are reducing microbial agents, as well as removing surface soil.

b. The description of cleaning and disinfecting (P6) blurs the differences between cleaning in the health care settings and in residences.

The first section in the discussion defines the goals of cleaning and disinfection procedures and raise concerns related to the high frequently of use of disinfectants in products investigated.

3. Literature review in introduction summarizes findings in relation to cleaning, but does not comment that none of the articles are about cleaning in hospitals or other health care institutions.

This is a pilot study of exposure assessment to cleaning products. We selected hospitals to study cleaning based in our hypotheses that hospital cleaning workers exposures are higher compared to residential cleaners. With these pilot data we are going a step further on testing this hypothesis. Further wider scale research is needed to assess exposures in health care settings. We have included one reference that relates asthma reports in health care industry (Pechter, 2005).

4. Tables 4 and 5 are labeled as potential and actual dermal exposures, but actual is not defined

Correct. We have changed the label. We have calculated only the *potential* exposures during cleaning tasks and not actual dermal exposures that take into account workers’ clothing, shoes and other PPE. For the epidemiologic investigations of health effects the actual dermal exposures must be calculated as individual workers will be assigned into different exposure categories. This is because the actual exposure calculations will need individual data on the PPE use.

5. Missing references

a. Vincent et al on page 3

Included in the discussion section.

b. Statement “ Dermal exposures to cleaning agents and related health impacts have been investigated by only a few studies” No reference provided.

Have changed the text.

Minor essential revisions.

We have addressed ALL identified typos and conducted additional language editing based on reviewer’s recommendations.

REVIWER 2: Jan-Paul Zock

Major Compulsory Revisions

1. The paper contains many valuable data but it is very long (perhaps too long) and is a mixture of a comprehensive review and some pilot studies. Authors should try to reduce the manuscript. Lots of information is spread over the introduction, results and discussion sections. Results, first part (hazardous ingredients ..) is an extensive review of a number of active ingredients. May be this information could be summarized in Table 3.

Agree. This study is an exposure assessment study and not a review study. We have reformulated the study’s background section to emphasize that. The data from other review studies are included in the discussion section.

We have summarized the health effect of the hazardous ingredients only on Table 3 and have deleted all the paragraphs in the text that provided the same information with this table. We have updated Table 3 with additional data.

The presentation of the DREAM assessment is out of the proportion given the limited attention in the text.

The application of the DREAM for cleaning tasks is an important part of the paper. We have included additional information for the DREAM with hope that this method can be used in the workplace exposure assessment to cleaning products.

Minor essential revisions

2. Introduction, page 4. In 2007 two papers were published on asthma in health care workers (1 from US and 1 from Europe), both identifying cleaning agents as risk factors. Authors may wish to quote these papers as they seem relevant for the topic under study.

We have included the following review papers:

- Rosenman KD: **Cleaning products-related asthma.** *Clinical Pulmonary Medicine* July 2006, **13**:221-228.
- Nielsen GD, Larsen ST, Olsen O, Lovik M, Poulsen LK, Glue C, Wolkoff P: **Do indoor chemicals promote development of airway allergy?** *Indoor Air* 2007, **17**:236-255.

3. Introduction page 7 second par., When reviewing the potential health effects of disinfectants, it could be helpful to identify irritant and sensitizing properties (instead of stating toxic properties).

Agree. We have corrected the language.

Discretionary revisions:

4. I am not sure whether is it appropriate to identify brand names (cleaning product manufacturers) as done here.

As suggested by the reviewer, we have deleted all identification of the manufactures.

5. Results, page 18 first group. Floor cleaning in hospitals is often done with bleach – containing products (but apparently not in the evaluated hospitals in Massachusetts. Although hypochlorite is not volatile, it is highly reactive and is likely to release secondary volatile exposures such as chloramines.

None of the hospitals in the study reported the use of chlorine. More data are necessary to generalize these findings.

Secondary emissions evaluations are important to consider for our future research on workplace exposure assessment. The case of secondary formation of chloramines and formaldehydes (which can be more hazardous than the parent compounds) indicate the need for re-designing of the traditional exposure assessment studies to more advance methods on exposure assessment that consider biological transformations of these chemicals in the body (biomarkers of exposure).

Reviewer 3: Peder Wolkoff.

General response.

The recent study by Rosenman, 2006 provides a comprehensive review of cleaning products and their potential health effects. Additionally Nielsen, 2007, evaluates agents in cleaning agents that may cause asthma. Both reviews emphasize the need for further research to understand the cause and the mechanism of asthma and respiratory symptoms among cleaners.

To our knowledge none of the existing epidemiologic studies that have investigated asthma and its relationship with cleaning products have conducted quantitative measures of cleaning related exposures. They have used qualitative exposure measures such as job title and product type. Better exposure metrics should be employed by the further epidemiological that will further shed the light on understanding the mechanism of asthma and respiratory symptoms among cleaners.

Qualitative investigation of the agents used in the workplace, and their application procedures is the first important step for identifying agents and tasks than can later be quantified in the workplace. With this manuscript we bring to the literature a list of the products used in the workplace and specify *the target* compounds for further exposure evaluation. In addition, we apply qualitative and semi- quantitative methods for assessing inhalation and dermal exposures. These methods can be used by epidemiological investigations as preferable compared to the crude exposure evaluations. Furthermore, the methods applied here can be used by the occupational health and safety professionals for workplace exposure prevention and control.

Our ultimate goal is to develop a strategy for quantitative exposure assessment to cleaning products. This manuscript is the first publication of our work that will be followed by two other manuscripts with focus on quantitative measures of exposures during common cleaning tasks.

Comments to the specific points:

Page 9. Identification of “hazardous” should be based on the cited literature documentation, TLV, or use of the data by the mouse bioassay (irritant). For example, if a compound is deemed a sensitizer, this should be documented, cf. (Dales et al 2004 and many others. Regarding 2) what is a “high” concentration? Regarding 4) quats are not volatile, but may be inhaled via aerosolization? Are all criteria (1-4) a prerequisite?

We made all the necessary changes to clarify the selection criteria based on reviewer’s comments. Additional literature has been cited in Table 3.

Because cleaning products contain many hazardous ingredients, it was important to identify the ingredients that are markers of exposure for the purpose of further exposure evaluation. The ingredients were selected by considering both a) the human health effects with respect to respiratory and dermal sensitization and irritation, and b) the potential for workplace exposures.

The first selection criterion considered selection of all frequently used ingredients concerning the degree of exposures in the workplace. Then, among all frequently found ingredients, we selected potential sensitizers and irritants (criteria 2). To identify

sensitizers and irritants, we conducted a review of the existing literature on *human* health effects of frequently used ingredients.

All known potential human sensitizers were selected and prioritized in the list; given the concern that sensitization may happen even at very low concentrations.

In the case of irritant ingredients further selection (criteria 3-4) considered their *relative* potential for workplace exposures, which were considered directly related to the ingredient's product concentrations and its volatility (relative to other mixture ingredients).

This strategy allowed *selection of* ingredients that were further evaluated for inhalation and dermal exposure potential using the selected qualitative /semi-qualitative methods.

Page 12-13

See results and discussion in Nielsen et al., 2007 a) and the above, including RD50 data and TLVs. I recommend downplaying case stories. The evaluation of the compounds needs to be much more thorough and semi-quantitative.

This is an exposure assessment study. Because cleaning products are mixtures of many chemical ingredients from different chemical classes, assessing and measuring exposures is very challenging. The strategy we followed in this study was to identify and prioritize "the most hazardous ingredients" based on the criteria that we defined. This task based exposure assessment strategy allowed us to *relatively* classify tasks for further exposure assessment and workplace control measures.

Classification of tasks in different exposure categories is a more powerful exposure metric compared to crude exposure measures such as "job title" that are currently used by epidemiological studies.

Characterization of exposures in relation to the existing occupational standards would require many assumptions. In our next manuscript we report actual airborne concentrations for the few target compounds identified here.

All boiling points should be deleted, they are in Table 3.

Yes. All the boiling points are included in Table 3.

Page 14

I do not understand why 2-BE is a low volatile compound. The distinction between, low, very low or high volatile is unclear.

There is different definition for what is a volatile organic compound (VOC). In general, substances that evaporate at the normal condition of temperature and pressure are VOCs. The definition is based on the compounds' boiling point (BP). Some countries define a VOC as an organic compound with a boiling point $<$ or $= 250^{\circ}\text{C}$. Others use $\text{BP}=200^{\circ}\text{C}$ as cut point. Wolkoff 1998 defines VOC as organic compounds with BP from 0- 400°C .

In this study we are relatively comparing different compounds based on their boiling points. Compounds with higher boiling points are considered "less "volatile than compounds with lower boiling points. Our goal is to relatively compare tasks based on the potential for the compounds to become airborne. We agree with reviewers' comments and have deleted the confusing language of "low "or "semi-volatile" ingredients.

Page 14-15

The presentation of the various compounds e.g isopropyl alcohol is trivial. These compounds should be much better characterized according to relevant health data.

We have revised Table 3 and have included all the known data related to health effects of human exposures to these chemicals. Most of the data are obtained in Toxnet (Hazardous Substances Data Base). When known RD50 were included.

Page 18.

The authors should use RD50 values and other relevant and documented data for the exposure evaluation. A simple semi-quantitative approach /condition should be applied. This could be:

A standard room with no air exchange, i.e static situation (max achievable concentration) or default exchange rate.

Instantaneous evaporation of all volatiles applied

Calculate max concentration and use this for semi-evaluation

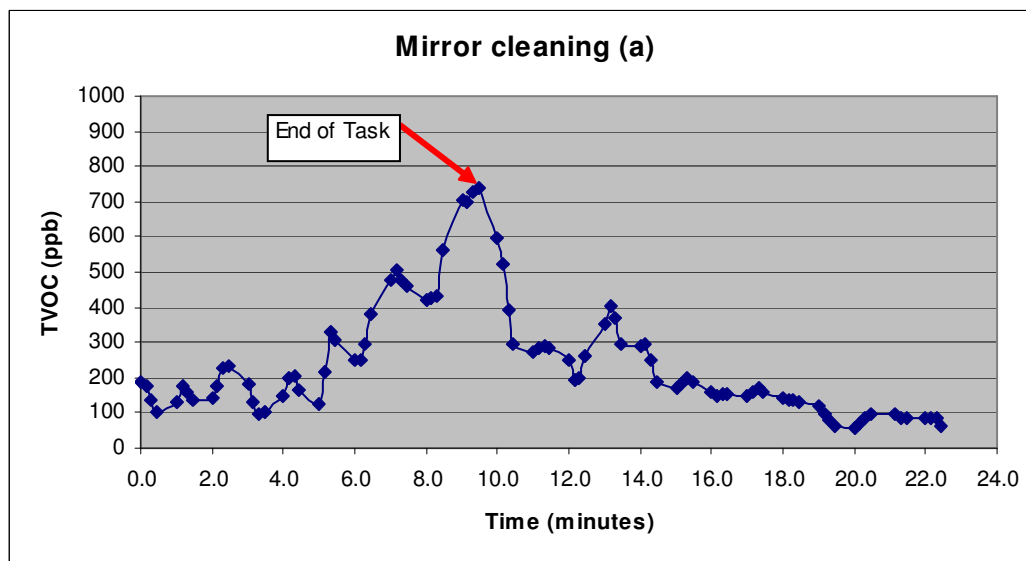
In addition, it should be taken into account that the evaporation of VOCs in aqueous solutions , in particular the polar ones, is delayed to after the evaporation of water, while the non-polar ones usually evaporate instantaneously upon application.

These recommendations are very important and can be applied to asses cleaning exposures in the workplace. They are based on several assumptions that will probably not hold in the workplace. Workplace exposure is very complex because the worker is involved in many cleaning task and uses many products continuously during the workday.

Our ultimate goal is to do a quantitative exposure assessment in the workplace. We propose a task-based exposure assessment because tasks are product specific and we can later assign exposures to workers based on the tasks he performs during the day. These methods can be used for epidemiological investigations and are very easy to use by occupational health professionals in the workplace.

We have prepared another manuscript that is ready for submission that focuses on quantitative assessment of cleaning tasks exposures. The manuscript will discuss the feasibility of measuring specific ingredients in the air during cleaning tasks. We have measured 2-BE and TVOC from cleaning tasks and report the actual concentrations levels in the air for the 10 minutes of simulated cleaning tasks. For example, average concentrations of TVOC measured for 10 minutes of cleaning tasks ranged from 0.14ppm to 11ppm and average concentrations of 2-BE measured during 10 minutes of cleaning tasks ranged from 0.30ppm to 21ppm. We also provide exposure TVOC profiles after the tasks.

The following is an example of the TVOC profiles during mirror cleaning.



There is a need for documentation that the aerosolized particles are respirable?

This is a very important topic that needs further evaluation. Aerosol sampling is necessary to assess the particle size and investigate if aerosolized particles from cleaning are respirable. We can not find any study that supports the hypotheses that aerosolized particles from cleaning are respirable.

Page 19:

Is there documentation that stripping and buffing will increase not only the concentration of particles, but they are respirable ?

Again – no documentation at this point- need further investigations to prove the hypotheses.

Page 21:

RD 50X 0.03 for 2-BE is 409 mg/m³, a rather high threshold concentration for sensory irritation. If we assume a 20 m³ room (4 by 2 by 2.5m) , no exchange rate and complete and instantaneous evaporation , this would equate to about 8.2 g applied to the pure compound. This would correspond to about 100g. solution -100ml for a 10% solution. As mentioned above , the evaporation of 2-BE will be delayed .I think this kind of exercises would be useful , at least for the volatile compounds, and including data form reported studies.

RD50 were missing for most of the compounds identified. In our next study we can compare the reviewer's recommended method and compare the results with actual measurements of 2-BE from cleaning tasks.

Quats should be discussed in contexts of Nielsen et al 2007a.

Nielsen, 2007 explanation of quats has been taken in consideration. At the end of his review he points that QACs are established as adjuvant in animal studies, supported by epidemiological studies. He suggests that exposures to quats may happen through inhalation exposures, which may be limited to occupational setting. Our work recommends further evaluation of *both* inhalation and dermal exposures to quats that may pose the risk not only to workers but other building occupants.

Several cases of reported aggravation of asthma: I doubt if such information is relevant without quantified documentation.

We agree and have deleted the reference. These are data from interviews with nurses that are not published yet in the literature.

Page 22:

It is likely that even concentrations above odor threshold may cause subjective sensory irritation, see also Shusterman 2007

Reference 42 deals with ultrafine formation in ozone –initiated limonene reactions, but not sensory irritation, at all.

In the last submitted manuscript reference # 41 (Wolkoff, 2006) was cited in relation to perceived sensory irritation because of the odor annoyance.

On the other hand, reference # 42 (Wainman 2000) was cited in relation to the secondary emissions from reactions with oxidants.

Page 23:

The discussion here about a two phase emission profile should be documented. The slow release of glycol ethers is probable, but disagrees with previous statements in the paper.

The slow release of glycol ethers from cleaning products has been investigated only by the experimental studies. To our knowledge, no field study has confirmed these results.

In our quantitative assessment (that will be presented in the next manuscript) we measured exposure profiles of TVOC during the performance of cleaning tasks simultaneously with 2-BE measures using integrated sampling & analytical methods (sorbets tubes + GC/MC). We observed that concentrations of 2- BE were higher compared to TVOC measured at the same. That indicated higher 2-BE concentration during product applications compared to other VOC in the air. We observed a two phase decay of TVOC concentrations after exposure cessation that is consistent with results from experimental studies. We could not obtain any data that prove that 2-BE was slowly released from surfaces in the air.

We have made the necessary language changes to address this concern.

That the volatiles should be judged according to their odor threshold, why it is so? And such odor threshold evaluation would be possible by the proposed above, provided state-of-the science odor thresholds are used.

The presence of odor indicates that compound is present in the air even at low concentrations. For the sensitizers this is important indication of risk given the fact that sensitization happens even at low concentration. For irritants: concentration above the odor thresholds have been related to perceived irritation. These subjective risks should be further evaluated and actual exposure levels are necessary to be measured and linked to reported irritation symptoms.

Tables, in general, contain a larger number of spelling mistakes, and should be checked carefully by an organic chemist.

Done.

Table 3: Formulas should be checked

RD50 and TLV values should be added where appropriate, and key literature

Relevant citations should be added for substantiation of statements

More consistent in reporting data , e.g regarding 2-BE : Has a boiling point ..and low volatility...

The formulations in inhalation exp, skin exp and sensitization should be normalized.

Done.