TOX/2022/30

Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment.

Introductory paper to an update of the COT position on aircraft cabin air

Introduction

1. In 2007, the Committee on Toxicity (COT) published a statement on aircraft cabin air, having been asked by the Department for Transport (DfT) to undertake an independent scientific review of data submitted by the British Airline Pilots Association (BALPA) relating to organophosphate (OP) compounds, the cabin air environment, ill-health in aircraft crews and the possible relationship to smoke/fume events in aircraft, due to concerns about the possible effects on aircrew health of oil/hydraulic fluid smoke/fume contamination incidents in commercial aircraft (COT, 2007).

2. In 2013, DfT asked the COT to undertake an independent scientific review of the results of DfT-funded aircraft cabin environment research commissioned in response to recommendations made by COT in 2007, after which the COT issued a position statement on cabin air (COT, 2013).

3. The COT has now been asked by DfT to investigate any new data have been published and to re-evaluate their previous view in the original statement from 2007 (<u>COT, 2007</u>) and position statement from 2013 (<u>COT, 2013</u>).

4. The scope of this follow-up work is to re-assess the overarching question on the potential health effects due to fume/contamination events, expanding the focus to include volatile organic compounds (VOCs) and semi-volatile organic compounds (sVOCs), on which there has been more focus in recent years.

Background

5. Between July 2006 and July 2007, the COT considered a referral from DfT to review data submitted by the BALPA due to concerns about possible effects on aircrew health following oil/hydraulic fluid smoke/fume contamination incidents in commercial aircraft. The objectives for COT were to evaluate the data sourced by BALPA to provide an independent scientific review of data due to concerns about the possible effects on aircrew health of oil/hydraulic fluid smoke/fume contamination incidents in commercial aircraft. The data submitted by BALPA related to OPs, the cabin air environment, ill-health in aircraft crews and the possible relationship to fume events in aircraft. A summary of the data considered by the Committee is provided in the 2007 COT statement (COT, 2007). The second objective was to provide DfT with appropriate advice on any further research required.

6. In the COT 2007/06 statement, the Committee concluded: "It was not possible on the basis of the available evidence in the BALPA submission or that sourced by the Secretariat and DH Toxicology Unit to conclude that there is a causal association between cabin air exposures (either general or following incidents) and ill-health in commercial aircraft crews. However, we noted a number of oil/hydraulic fluid smoke/fume contamination incidents where the temporal relationship between reports of exposure and acute health symptoms provided evidence that an association was plausible" (COT, 2007).

7. Regarding health, it was noted that there was insufficient evidence available to the Committee to recommend additional epidemiological research on acute health effects or specifically on OPs. However, the need to obtain objective measures of exposure in epidemiology studies was acknowledged, and this could be achieved using exposure monitoring via proxy measures of exposure. There was also insufficient evidence to recommend additional research relating to acute or chronic health effects with regard to oil/hydraulic fluid contamination incidents on commercial aircraft, although the limited evidence and information on pilots supported further investigation into potential neuropsychological impairment in commercial pilots. This could be achieved by carrying out a cross-sectional study, comparing results of neuropsychological testing between pilots flying different airframes/engine combinations and between pilots who report, or do not report, air quality incidents.

Use of a validated proxy exposure for oil/hydraulic fluid contamination exposure would be necessary in order to determine whether there is an association between oil/hydraulic fluid smoke/fume contamination and neuropsychological effects (<u>COT</u>, <u>2007</u>).

8. To address recommendations made by COT, DfT commissioned four studies, namely: the identification of air monitoring equipment capable of sampling air during fume events in real time; a statistical analysis of data relating to fume events and operational parameters in aircraft to investigate a potential link between cabin air fume events and aircraft full power take-offs; real time in-flight cabin air sampling and data analysis; and an investigation of aircraft cabin surface residues. These projects aimed to assess airborne concentrations and surface deposition of chemical pollutants in the cabins of commercial aircraft, and to investigate operational parameters associated with fume events.

9. In 2013, COT reviewed a discussion paper on exposure monitoring of the aircraft cabin environment, covering the four projects commissioned by DfT. The Committee also considered papers that had been published in the peer-reviewed scientific literature since 2007, concerning exposures to chemical pollutants in aircraft cabins (TOX/2013/32).

10. In 2013, COT also produced a position paper on cabin air that summarised the Committees evaluation of the four study reports, the conclusions drawn from the evidence considered to date, the scientific uncertainties that remained, and options for further research to address the continuing uncertainties (<u>COT, 2013</u>). The Committee agreed several conclusions relating to health:

- "The acute illness which has occurred in relation to perceived episodes of contamination might reflect a toxic effect of one or more chemicals, but it could also have occurred through nocebo effects".
- "While there is strong scientific evidence that nocebo effects can lead to (sometimes severely disabling) illness from environmental exposures that are perceived as hazardous, there is no simple and reliable way of establishing that nocebo responses are responsible for individual cases of illness. However, they are a plausible alternative explanation if toxicity seems

unlikely. Distinguishing whether acute illness from fume events is likely to arise from toxicity or nocebo responses depends on: assessment of the patterns of symptoms and clinical abnormalities in affected individuals; the levels of relevant chemicals to which they might have been exposed; and what is known about the toxic effects of those chemicals and the levels of exposure at which such toxic effects occur (including the possibility that some individuals might be unusually sensitive)".

- "The patterns of illness that have been reported following fume events do not conform with that which would be expected from exposure to triaryl phosphates such as ortho-tricresyl phosphate (o-TCP) (which differs from the pattern of illness that occurs with over-exposure to organophosphate insecticides and nerve agents). Over-exposure to tricresyl phosphates would be expected to cause delayed peripheral neuropathy. Given the short duration of reported fume incidents, in order to cause such toxicity, peak exposures would have to be much higher than those which have been indicated by monitoring to date".
- "More generally, the Committee considers that a toxic mechanism for the illness that has been reported in temporal relation to fume incidents is unlikely. Many different chemicals have been identified in the bleed air from aircraft engines, but to cause serious acute toxicity, they would have to occur at very much higher concentrations than have been found to date (although lower concentrations of some might cause an odour or minor irritation of the eyes or airways). Furthermore, the symptoms that have been reported following fume incidents have been wide-ranging (including headache, hot flushes, nausea, vomiting, chest pain, respiratory problems, dizziness and light-headedness), whereas toxic effects of chemicals tend to be more specific. However, uncertainties remain, and a toxic mechanism for symptoms cannot confidently be ruled out".

11. Overall, the Committee stated: "Finally, it should be emphasised that illness can be disabling whether it occurs through toxicity or through nocebo effects, and therefore there is a continuing imperative to minimise the risk of fume incidents that give rise to symptoms" (<u>COT, 2013</u>).

Current paper

12. The current paper is a scoping paper to outline literature searches carried out to update the evidence base and to outline potential future work.

13. An update of the literature searches previously undertaken between 2007 and 2013 regarding health effects in flight crew following exposure to aircraft cabin environments and the potential relationship to smoke/fume events in aircraft is presented. Literature searches were carried out using the original search terms, focussing on literature published during 2007-2021. The searches were limited to the chemicals included in the original searches, which largely focussed on OP-type chemicals. Five additional papers were identified from the title and abstract as possibly being of relevance. A short narrative of each paper is presented below (paragraph 15 - 21.

14. A literature search was also carried out to identify exposure data for VOCs and sVOCs in modes of transport, including aircraft, and indoor work environments such as offices, to allow comparison between different environments. Results of such searches are presented below (paragraph 22 - 27).

Updated literature search on OPs (2007-2021)

15. Search terms used previously were replicated; inclusion and exclusion criteria and the search results are presented in Annex 1 to this paper.

16. Five new papers were identified that assessed the health effects in flight crew following exposure to OPs from fume events.

17. de Boer et al. (2015) noted that airline pilots reported loss of memory, headaches, dizziness, tunnel vision and other neurotoxic effects, despite levels of TCP in flight deck air not exceeding provisional toxicity thresholds. It was suggested that TCP on its own is not likely to be responsible for the reported health effects.

18. de Ree et al. (2014) reported that TCP has been suggested to be associated with the alleged 'aerotoxic syndrome', the symptoms of which include headaches, loss of balance, numbress and neurobehavioral abnormalities such as emotional

instability, depression and cognitive dysfunction. Measurements of non-ortho and ortho-isomers were monitored in aircraft and showed the presence of non-toxic nonortho isomers at low concentrations. However, tri-ortho-cresyl phosphate (ToCP) and other ortho-isomers were not detected. The authors concluded that it is unlikely that health effects and aerotoxic syndrome are due to exposure to ToCP.

19. Heutelbeck et al. (2016) investigated individual acetylcholinesterase (AChE) and neuropathy target esterase (NTE) activities in flight crew members exhibiting headache, cognitive difficulties, and neurological disorder after fume events. Using biochemical effect monitoring, the measured AChE activities indicated a minor contribution of OP or related compounds to the observed activities. The authors concluded that it was not possible to infer a direct correlation between manifestations and AChE-inhibiting compounds.

20. Wolkoff, Crump and Harrison (2016) carried out a review of sensory effects in the eyes and airways and neurological symptoms such as headache reported in aircraft crew and office workers and their possible association with VOC and ToCP exposure. Despite using a conservative approach to assess any correlation, the authors concluded that the health risk of exposure to ToCP in aircraft is negligible.

21. Reneman et al. (2016) recorded more self-reported cognitive complaints and depressive symptoms in two flight crew subjects compared with two controls. Subjects also showed small clusters in the brain where white matter microstructure was affected, higher cerebral perfusion values in the left occipital cortex, and reduced brain activation on a functional magnetic resonance imaging (MRI) executive function task. It was concluded that the extent of cognitive impairment was strongly associated with white matter integrity, but the extent of estimated number of flight hours was not associated with cognitive impairment nor with reductions in white matter microstructure.

Literature search on exposure to VOCs in modes of transport

22. A literature search was carried out to collate exposure data on VOCs in aircraft in comparison with other modes of transport such as cars, buses, trains, taxis

and metros. The search terms used for the literature search are presented in Annex 2.

23. Forty-one papers were identified. Two papers related to vehicles in general, six papers related to exposure to VOCs in buses, two papers each in metros and taxis, three paper in trains and thirteen papers each in cars and aircraft. A list of all publications is given in Annex 2.

Literature search on exposure to VOCs in other work environments

24. A literature search was carried out to investigate how exposure to VOCs in aircraft compared with that in other public spaces such as offices, schools and hospitals. The search terms used for the literature search are presented in Annex 3.

25. Thirty-two papers were identified. All 32 related to exposure in offices, while six papers also addressed exposure in schools and one reported exposure in hospitals. A list of all publications is given in Annex 3.

Future work planned

26. A number of papers are planned for the future, including:

- Definition of a fume/contamination event and identification and levels of chemicals measured in such events
- Narrative of papers identified in searches carried out for this scoping paper regarding exposure data on VOC/sVOCs in aircraft cabins, and comparison with exposure in other modes of transport and indoor work environments such as offices
- Comparison of adverse health effects reported in aircraft cabin workers and office workers
- Identification of VOC/sVOCs of particular interest
- Toxicological review of VOC/sVOCs of interest, including collation or derivation of health-based guidance values

- Health effects of mixture of VOC/sVOCs, using COT papers on mixtures, EFSA review of combinations of chemicals, and Working Group on Pesticides (WGP) papers as information sources
- Narrative of papers identified in the original and updated searches on OPs in cabin air.

Questions on which the views of the Committee are sought

27. Members are invited to consider this paper and in particular the following questions:

- i. Do Members have any comments on the searches undertaken to date?
- ii. Do Members have any suggestions for other aspects to consider to support the Committee consideration of this topic in the coming meetings?

IEH Consulting under contract supporting the PHE COT Secretariat May 2022

References

- COT, 2007. Statement on the review of the cabin air environment, ill-health in aircraft crews and the possible relationship to smoke/fume events in aircraft. COT 2007/06. <u>https://webarchive.nationalarchives.gov.uk/ukgwa/20200803163453mp_/https</u> ://cot.food.gov.uk/sites/default/files/cotstatementbalpa200706.pdf
- COT, 2013a. Discussion paper on exposure monitoring of the aircraft cabin environment. TOX/2013/32. <u>https://cot.food.gov.uk/sites/default/files/cot/tox201332.pdf</u>
- COT, 2013b. Annex 6. Discussion paper on exposure monitoring of the aircraft cabin environment. TOX/2013/32. Annex 6. <u>https://cot.food.gov.uk/sites/default/files/cot/tox32anex6.pdf</u>
- COT, 2013. Position paper on cabin air. <u>https://webarchive.nationalarchives.gov.uk/ukgwa/20200803134320/https:/cot</u> <u>.food.gov.uk/cotstatements/cotstatementsyrs/cotstatements2013/cotpospacab</u> <u>air</u>
- de Boer, J., A. Antelo, I. van der Veen, S. Brandsma & N. Lammertse (2015)
 Tricresyl phosphate and the aerotoxic syndrome of flight crew members Current gaps in knowledge. *Chemosphere*, 119, S58.
- de Ree, H., M. van den Berg, T. Brand, G. J. Mulder, R. Simons, B. Veldhuijzen van Zanten & R. H. S. Westerink (2014) Health risk assessment of exposure to TriCresyl Phosphates (TCPs) in aircraft: A commentary. *NeuroToxicology*, 45, 209-215.
- Heutelbeck, A. R. R., C. Bornemann, M. Lange, A. Seeckts & M. M. Mueller (2016)
 Acetylcholinesterase and neuropathy target esterase activities in 11 cases of symptomatic flight crew members after fume events. *J. Toxicol. Environ. Health, Part A*, 79, 1050-1056.

- Reneman, L., S. B. Schagen, M. Mulder, H. J. Mutsaerts, G. Hageman & M. B. de Ruiter (2016) Cognitive impairment and associated loss in brain white microstructure in aircrew members exposed to engine oil fumes. *Brain Imaging Behav*, 10, 437-444.
- Wolkoff, P., D. R. Crump & P. T. C. Harrison (2016) Pollutant exposures and health symptoms in aircrew and office workers: Is there a link? *Environ. Int.*, 87, 74-84.

AChE	Acetylcholinesterase
BALPA	British Airline Pilots Association
СОТ	Committee on Toxicity
DfT	Department for Transport
DH	Department of Health
MRI	Magnetic resonance imaging
NTE	Neuropathy target esterase
OP	Organophosphate
o-TCP	Ortho-tricresyl phosphate
sVOC	Semi-volatile organic compounds
ТоСР	Tri-ortho-cresyl phosphate
VOC	Volatile organic compounds
WGP	Working Group on Pesticides

List of Abbreviations and Technical terms

TOX/2022/30 ANNEX A

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Introductory paper to an update of the COT position on aircraft cabin air

Introduction

1. The COT was asked to update the literature searches previously carried out between 2007 and 2013 regarding air quality in aircraft cabin environments and the potential relationship to smoke/fume events in aircraft and health effects in cabin crew focussing on organophosphates (OPs).

2. Search terms presented in TOX/2013/32 Annex 6 were replicated for the searches. Inclusion and exclusion criteria used in TOX/2013/32 Annex 6 were amended and included the following:

3. Inclusion criteria

- Peer reviewed publications
- Relevant reviews
- In PubMed, search terms in title and abstract
- In SciFinder, search terms in all fields
- Papers from 2013 to present
- 4. Exclusion criteria
 - Studies not reporting original results, including comments, letters or editorials
 - Papers without an abstract

- Papers concerned only with methodology
- Studies reporting animal or *in vitro* data
- Studies dealing only with health outcomes or biomonitoring
- Studies dealing with exposures other than those relating to chemical exposure from oil/hydraulic fluid and flame retardants, for example tobacco smoke, solar radiation, infectious disease particles, ozone, pesticides
- Papers dealing with organophosphates previously reviewed by COT
- Conflicting abbreviations such as BDPP (bioactive dietary polyphenol preparation), DBPP (diastolic blood pressure percentile), TCP (transscleral cyclophotocoagulation) and TBP (treated beyond progression or TATA box-binding protein or tuberculous pleuritis)

5. The number of publications considered to be relevant, based on the title and abstract, from current and previous searches are presented in Table 1. The current searches were carried out using PubMed and SciFinder whereas the previous searches were carried out using PubMed and Web of Science.

Table 1Literature searches in PubMed (2007-2013 and 2013-present), Web of Science (2007-2013) and SciFinder
(2013-present)

		PubMed	Web of	PubMed	PubMed	SciFinder	SciFinder	PubMed +
			Science					SciFinder
	Search Terms/ Details	Relevant	Relevant	No. of	Relevant	No. of	Relevant	Total no.
		references	references	references	references	references	references	of relevant
		2007-2013	2007-2013	retrieved	2013-	retrieved	2013-	references
				2013-	present	2013-	present	2013-
				present		present		present**
1	Cabin air	4	4	44	6	99	5	8
2	Cabin air quality	1	1	10	0	23	0	0
3	Aircraft air contamination	2	2	0	0	0	0	0
4	Butyl diphenyl phosphate	0	0	0	0	9	0	0
5	Dibutylphenyl phosphate	1	2	0	0	1	0	0
6	Tri-ortho-cresyl phosphate	2	0	27	1	30	4	4
7	Tri-cresyl phosphate	0	0	6	0	9	0	0
8	Tricresyl phosphate	4	4	60	1	518	5	5
9	Tributyl phosphate	0	2	124	0	1845	0	0

10	Tri-ortho-cresyl phosphate	2	0	3	0	8*	0	0
	AND aircraft							
11	Toluene AND aircraft	0	2	2	0	297	0	0
12	Xylene AND aircraft	0	2	0	0	130	0	0
13	Limonene AND aircraft	0	0	0	0	15	0	0
14	Undecane AND aircraft	0	0	1	0	31	1	1
15	Tributyl phosphate AND	0	0	3	0	8	0	0
	aircraft							
16	Tricresyl phosphate AND	0	4	14	2	21	4	4
	aircraft							
17	Butyl diphenyl phosphate AND	0	0	0	0	0	0	0
	aircraft							
18	Dibutylphenyl phosphate AND	1	2	0	0	0	0	0
	aircraft							
19	Aircraft AND fume(s)	1	0	8	2	16	3	4
20	Aircraft AND oil	3	4	59	3	708	1	4
21	Air quality AND (airline OR	1	4	78	0	317	0	0
	airplane OR aircraft OR cockpit							
	OR "passenger cabin" OR							
	flight deck)							

22	Aircrew OR "airline crew" OR	1	3	764	1	812	0	1
	"cabin attendants" OR "cabin							
	crew" OR "cockpit crew" OR							
	"crew members" OR "flying							
	crew" OR "flight engineers" OR							
	"flight attendants" OR flight							
	deck OR "airline pilots" OR							
	"aircraft pilots" OR "airplane							
	pilots" OR stewardesses OR							
	"flight deck crew" NOT "aircraft							
	carrier"							
23	(aircrew OR "airline crew" OR	1	3	45	0	65	0	0
	"cabin attendants" OR "cabin							
	crew" OR "cockpit crew" OR							
	"crew members" OR "flying							
	crew" OR "flight engineers" OR							
	"flight attendants" OR flight							
	deck OR "airline pilots" OR							
	"aircraft pilots" OR "airplane							
	pilots" OR stewardesses OR							
	"flight deck crew" NOT "aircraft							

	carrier") AND (fume OR fumes							
	OR smoke OR haze OR mist							
	OR smell OR smells OR odor*							
	OR odour* OR vapor* OR dust							
	OR aerosol* OR gas OR							
	gases)							
24	Air quality AND airport	0	13	44	0	87	0	0
25	Air quality AND "airport	0	0	0	0	0	0	0
	building" OR "airport buildings"							
25	Air quality AND "airport offices"	0	0	0	0	0	0	0
26	Cabin air AND flame retardant	0	2	2	1	3	1	1
27	Aircraft and flame retardant	3	3	12	0	35	0	0
28	Toluene AND indoor air	1	0	139	0	591	0	0
29	Xylene AND indoor air	1	0	71	0	12	0	0
30	Tributyl phosphate AND indoor	0	0	5	0	75	0	0
	air							
31	Tricresyl phosphate AND	0	0	0	0	38	0	0
	indoor air							

*2013-2016

**With duplicates removed

Results

- 6. Of the 26 papers identified, five are considered to be of relevance:
 - de Boer, J., A. Antelo, I. van der Veen, S. Brandsma & N. Lammertse (2015) Tricresyl phosphate and the aerotoxic syndrome of flight crew members - Current gaps in knowledge. *Chemosphere*, 119, S58.
 - de Ree, H., M. van den Berg, T. Brand, G. J. Mulder, R. Simons, B. Veldhuijzen van Zanten & R. H. S. Westerink (2014) Health risk assessment of exposure to TriCresyl Phosphates (TCPs) in aircraft: A commentary. *NeuroToxicology*, 45, 209-215.
 - Heutelbeck, A. R. R., C. Bornemann, M. Lange, A. Seeckts & M. M. Mueller (2016) Acetylcholinesterase and neuropathy target esterase activities in 11 cases of symptomatic flight crew members after fume events. *J. Toxicol. Environ. Health, Part A,* 79, 1050-1056.
 - Reneman, L., S. B. Schagen, M. Mulder, H. J. Mutsaerts, G. Hageman & M. B. de Ruiter (2016) Cognitive impairment and associated loss in brain white microstructure in aircrew members exposed to engine oil fumes. *Brain Imaging Behav*, 10, 437-444.
 - Wolkoff, P., D. R. Crump & P. T. C. Harrison (2016) Pollutant exposures and health symptoms in aircrew and office workers: Is there a link? *Environ. Int.*, 87, 74-84.

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TOX/2022/30 ANNEX B

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Introductory paper to an update of the COT position on aircraft cabin air

Literature searches for exposure to VOCs in other modes of transport

Search terms

1. Search terms for Scopus and PubMed are presented below.

Scopus

(TITLE-ABS-KEY ("volatile organic compound*" OR "semivolatile organic compound*" OR vocs OR svocs) AND TITLE-ABS-KEY ("public transport*" OR taxi* OR car OR cars OR bus OR buses OR train OR trains OR aeroplane* OR aircraft* OR submarine* OR boat* OR ship OR ships)) AND PUBYEAR > 2012 AND PUBYEAR < 2022 AND (LIMIT-TO (LANGUAGE , "English") OR EXCLUDE (LANGUAGE , "French")): 954

PubMed

(("volatile organic compound*"[Title/Abstract] OR VOCs[Title/Abstract] OR sVOCs[Title/Abstract] OR "semivolatile organic compound*"[Title/Abstract]) OR (compounds, volatile organic OR organic compounds, volatile[MeSH Terms])) AND ("public transport*" [Title/Abstract] OR taxi* [Title/Abstract] OR car [Title/Abstract] OR cars [Title/Abstract] OR taxi* [Title/Abstract] OR car [Title/Abstract] OR cars [Title/Abstract] OR bus [Title/Abstract] OR buses [Title/Abstract] OR train [Title/Abstract] OR trains [Title/Abstract] OR aeroplane* [Title/Abstract] OR aircraft* [Title/Abstract] OR submarine* [Title/Abstract] OR boat* [Title/Abstract] OR ship [Title/Abstract] OR ships[Title/Abstract] AND ((2013/1/1:2021/12/31[pdat]) AND (english[Filter]))): 273

- 2. Inclusion criteria
 - Peer reviewed publications
 - Relevant reviews
 - In PubMed, search terms in title and abstract
 - In Scopus, search terms in all fields
 - Papers from 2013 to present
- 3. Exclusion criteria
 - Studies not reporting original results, including comments, letters or editorials
 - Papers without an abstract
 - Papers concerned only with methodology
 - Studies dealing only with health outcomes or biomonitoring
 - Conflicting abbreviations such as BDPP (bioactive dietary polyphenol preparation), DBPP (diastolic blood pressure percentile), TCP (transscleral cyclophotocoagulation) and TBP (treated beyond progression or TATA box-binding protein or tuberculous pleuritis)

Results

4. Forty-one papers were identified.

5. Two papers related to vehicles in general (Do et al. 2014, Xu, Chen and Xiong 2018).

6. Six papers related to exposure to VOCs in buses (Cheng, Yen and Li, Gastelum-Arellanez et al. 2021, Kim 2020, Lin et al. 2020, Moolla, Curtis and Knight 2015a, Moolla, Curtis and Knight 2015b).

7. Two papers related to metros (Passi, Nagendra and Maiya 2021, Xu and Hao 2017).

8. Two papers related to taxis (Bakhtiari et al. 2018, Moreno et al. 2019),

9. Three papers related to trains (Awang, Isah and Hamid 2015, Awang et al. 2014, Maggos et al. 2016).

10. Thirteen papers related to cars (Ali et al. 2021, Brodzik et al. 2014, Faber and Brodzik 2017, Gong et al. 2017, Gong et al. 2019, Kim, Park and Lee 2019, Kim et al. 2016, Lexén et al. 2021, Ren et al. 2017, Siripongpokin et al. 2014, Yassin, Ramadan and Alshammari , Yue et al. 2017, Zulauf et al. 2019)

11. Thirteen papers related to aircraft (Chen et al. 2021, Cross et al. 2013, Guan et al. 2014a, Guan, Li and Yang 2015, Guan et al. 2014b, Guan, Yang and Li , Mokalled et al. 2019, Schuchardt, Koch and Rosenberger 2019, Wang et al. 2014a, Wang et al. 2014b, Wolkoff, Crump and Harrison 2016, Yang et al. 2018, Zubair, Ahmad and Riazuddin 2014).

Papers

- Ali, N., M. W. Kadi, H. M. S. Ali Albar, M. I. Rashid, S. Chandrasekaran, A. S. Summan, C. A. de Wit & G. Malarvannan (2021) Semi-volatile organic compounds in car dust: A pilot study in jeddah, saudi arabia. *International Journal of Environmental Research and Public Health*, 18.
- Awang, N., S. A. Isah & A. Hamid (2015) Cytogenetic analysis among train depot workers exposed to total volatile organic compounds. *OnLine Journal of Biological Sciences*, 15, 53-58.
- Awang, N., N. F. Mohd. Alwi, S. Hajar Yaacob & I. Ishak (2014) A study on exposure to air pollutants and their effects to the respiratory level

This is a preliminary paper for discussion. It does not represent the views of the Committee and must not be quoted, cited or reproduced. among employees of Sentul Railway Electric Multiple Unit (EMU) depot. World Applied Sciences Journal, 29, 402-407.

- Bakhtiari, R., M. Hadei, P. K. Hopke, A. Shahsavani, N. Rastkari, M. Kermani, M. Yarahmadi & A. Ghaderpoori (2018) Investigation of in-cabin volatile organic compounds (VOCs) in taxis; influence of vehicle's age, model, fuel, and refueling. *Environmental Pollution*, 237, 348-355.
- Brodzik, K., J. Faber, D. Łomankiewicz & A. Gołda-Kopek (2014) Invehicle VOCs composition of unconditioned, newly produced cars. *Journal of Environmental Sciences (China)*, 26, 1052-1061.
- Chen, R., L. Fang, J. Liu, B. Herbig, V. Norrefeldt, F. Mayer, R. Fox & P. Wargocki (2021) Cabin air quality on non-smoking commercial flights: A review of published data on airborne pollutants. *Indoor air,* 31, 926-957.
- Cheng, Y. H., G. W. Yen & A. C. Li. Short-term exposure to volatile organic compounds for passengers at two intercity bus terminals.
- Cross, E. S., J. F. Hunter, A. J. Carrasquillo, J. P. Franklin, S. C. Herndon, J. T. Jayne, D. R. Worsnop, R. C. Miake-Lye & J. H. Kroll (2013) Online measurements of the emissions of intermediate-volatility and semi-volatile organic compounds from aircraft. *Atmospheric Chemistry and Physics*, 13, 7845-7858.
- Do, D. H., H. Van Langenhove, S. I. Chigbo, A. N. Amare, K.
 Demeestere & C. Walgraeve (2014) Exposure to volatile organic compounds: Comparison among different transportation modes.
 Atmospheric Environment, 94, 53-62.
- Faber, J. & K. Brodzik (2017) Air quality inside passenger cars. *AIMS Environmental Science*, 4, 112-133.

- Gastelum-Arellanez, A., J. Esquivel-Días, R. Lopez-Padilla, V. H. Robledo, R. Paulina, M. F. Beltrán & J. O. Saucedo-Lucero (2021) Assessment of persistent indoor VOCs inside public transport during winter season. *Chemosphere*, 263.
- Gong, Y., Y. Wei, J. Cheng, T. Jiang, L. Chen & B. Xu (2017) Health risk assessment and personal exposure to Volatile Organic Compounds (VOCs) in metro carriages — A case study in Shanghai, China. *Science of the Total Environment*, 574, 1432-1438.
- Gong, Y., T. Zhou, Y. Zhao & B. Xu (2019) Characterization and risk assessment of particulate matter and volatile organic compounds in metro carriage in Shanghai, China. *Atmosphere*, 10.
- Guan, J., K. Gao, C. Wang, X. Yang, C. H. Lin, C. Lu & P. Gao (2014a) Measurements of volatile organic compounds in aircraft cabins. Part I: Methodology and detected VOC species in 107 commercial flights. *Building and Environment*, 72, 154-161.
- Guan, J., Z. Li & X. Yang (2015) Net in-cabin emission rates of VOCs and contributions from outside and inside the aircraft cabin. *Atmospheric Environment*, 111, 1-9.
- Guan, J., C. Wang, K. Gao, X. Yang, C. H. Lin & C. Lu (2014b) Measurements of volatile organic compounds in aircraft cabins. Part II: Target list, concentration levels and possible influencing factors. *Building and Environment*, 75, 170-175.
- Guan, J., X. Yang & Z. Li. Source contributions and control strategies of volatile organic compounds (VOCS) in aircraft cabins. 727-734.
- Kim, H. H. (2020) Characteristics of exposure and health risk air pollutants in public buses in Korea. *Environmental Science and Pollution Research*, 27, 37087-37098.

- Kim, H. H., G. Y. Park & J. H. Lee (2019) Concentrations of particulate matter, carbon dioxide, VOCs and risk assessment inside Korean taxis and ships. *Environmental Science and Pollution Research*, 26, 9619-9631.
- Kim, K. H., J. E. Szulejko, H. J. Jo, M. H. Lee, Y. H. Kim, E. Kwon, C. J. Ma & P. Kumar (2016) Measurements of major VOCs released into the closed cabin environment of different automobiles under various engine and ventilation scenarios. *Environmental Pollution*, 215, 340-346.
- Lexén, J., M. Bernander, I. Cotgreave & P. L. Andersson (2021) Assessing exposure of semi-volatile organic compounds (SVOCs) in car cabins: Current understanding and future challenges in developing a standardized methodology. *Environment international*, 157.
- Lin, C. C., G. W. Yen, Y. H. Cheng & R. H. Shie (2020) Exposure levels of volatile organic compounds and potential health risks for passengers and workers at an intercity bus terminal. *Atmospheric Pollution Research*, 11, 1820-1828.
- Maggos, T., D. Saraga, K. Bairachtari, I. Tzagkaroulaki, S. Pateraki, C. Vasilakos, C. Makarounis, A. Stavdaris, G. Danias, G. Anagnostopoulos & V. Frountas (2016) Air quality assessment in passenger trains: the impact of smokestack emissions. *Air Quality, Atmosphere and Health,* 9, 391-401.
- Mokalled, T., J. Adjizian Gérard, M. Abboud, C. Trocquet, R. Nassreddine, V. Person & S. le Calvé (2019) VOC tracers from aircraft activities at Beirut Rafic Hariri International Airport. *Atmospheric Pollution Research*, 10, 537-551.
- Moolla, R., C. J. Curtis & J. Knight (2015a) Assessment of occupational exposure to BTEX compounds at a bus diesel-refueling bay: A case

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study in Johannesburg, South Africa. Science of the Total Environment, 537, 51-57.

- --- (2015b) Occupational exposure of diesel station workers to BTEX compounds at a bus depot. *International Journal of Environmental Research and Public Health*, 12, 4101-4115.
- Moreno, T., A. Pacitto, A. Fernández, F. Amato, E. Marco, J. Grimalt, G. Buonanno & X. Querol (2019) Vehicle interior air quality conditions when travelling by taxi. *Environmental research*, 172, 529-542.
- Passi, A., S. M. S. Nagendra & M. P. Maiya (2021) Characteristics of indoor air quality in underground metro stations: A critical review. *Building and Environment*, 198.
- Ren, J., S. Xu, X. Liu, W. Liu & E. Cui. 2017. Research on the present situation and factors of volatile organic compounds in car cabin. 67-74.
- Schuchardt, S., W. Koch & W. Rosenberger (2019) Cabin air quality Quantitative comparison of volatile air contaminants at different flight phases during 177 commercial flights. *Building and Environment*, 148, 498-507.
- Siripongpokin, P., V. Cheevaporn, N. Tangkrock-Olan & H. F. Helander (2014) Health risk assessment and DNA damage of volatile organic compounds in car painting houses. *EnvironmentAsia*, 7, 142-151.
- Wang, C., X. Yang, J. Guan, K. Gao & Z. Li (2014a) Volatile organic compounds in aircraft cabin: Measurements and correlations between compounds. *Building and Environment*, 78, 89-94.
- Wang, C., X. Yang, J. Guan, Z. Li & K. Gao (2014b) Source apportionment of volatile organic compounds (VOCs) in aircraft cabins. *Building and Environment*, 81, 1-6.

- Wolkoff, P., D. R. Crump & P. T. C. Harrison (2016) Pollutant exposures and health symptoms in aircrew and office workers: Is there a link? *Environment international*, 87, 74-84.
- Xu, B., X. Chen & J. Xiong (2018) Air quality inside motor vehicles' cabins: A review. *Indoor and Built Environment*, 27, 452-465.
- Xu, B. & J. Hao (2017) Air quality inside subway metro indoor environment worldwide: A review. *Environment international*, 107, 33-46.
- Yang, X., S. Cheng, J. Lang, R. Xu & Z. Lv (2018) Characterization of aircraft emissions and air quality impacts of an international airport. *Journal of Environmental Sciences (China)*, 72, 198-207.
- Yassin, M. F., A. Ramadan & B. Z. Alshammari. Volatile organic compounds in car parking and its effect on human health. 629-633.
- Yue, T., X. Yue, F. Chai, J. Hu, Y. Lai, L. He & R. Zhu (2017) Characteristics of volatile organic compounds (VOCs) from the evaporative emissions of modern passenger cars. *Atmospheric Environment*, 151, 62-69.
- Zubair, M., K. A. Ahmad & V. N. Riazuddin. 2014. A review on the impact of aircraft cabin air quality and cabin pressure on human wellbeing. 388-394.
- Zulauf, N., J. Dröge, D. Klingelhöfer, M. Braun, G. M. Oremek & D. A. Groneberg (2019) Indoor air pollution in cars: An update on novel insights. *International Journal of Environmental Research and Public Health,* 16.

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TOX/2022/30 ANNEX C

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

Introductory paper to an update of the COT position on aircraft cabin air

Literature searches for exposure to VOCs in indoor work environments such as offices

Search terms

1. Search terms for Scopus and PubMed are presented below.

Scopus

(TITLE-ABS-KEY ("volatile organic compound*" OR "semivolatile organic compound*" OR vocs OR svocs) AND TITLE-ABS-KEY ("office OR work place)) AND PUBYEAR > 2012 AND PUBYEAR < 2022 AND (LIMIT-TO (LANGUAGE, "English") OR EXCLUDE (LANGUAGE, "French"))

PubMed

(("volatile organic compound*"[Title/Abstract] OR VOCs[Title/Abstract] OR sVOCs[Title/Abstract] OR "semivolatile organic compound*"[Title/Abstract]) OR (compounds, volatile organic OR organic compounds, volatile[MeSH Terms])) AND ("office" [Title/Abstract] OR work place [Title/Abstract] AND ((2013/1/1:2021/12/31[pdat]) AND (english[Filter])))

- 2. Inclusion criteria
 - Peer reviewed publications
 - Relevant reviews

- In PubMed, search terms in title and abstract
- In Scopus, search terms in all fields
- Papers from 2013 to present
- 3. Exclusion criteria
 - Studies not reporting original results, including comments, letters or editorials
 - Papers without an abstract
 - Papers concerned only with methodology
 - Studies dealing only with health outcomes or biomonitoring
 - Conflicting abbreviations such as BDPP (bioactive dietary polyphenol preparation), DBPP (diastolic blood pressure percentile), TCP (transscleral cyclophotocoagulation) and TBP (treated beyond progression or TATA box-binding protein or tuberculous pleuritis)

Results

- 4. Thirty-two papers were identified.
- 5. All 32 papers related to office environments.

6. Six papers related to exposure in schools (Cometto-Muñiz and Abraham 2015, Faria et al. 2016, Goodman et al., Lucattini et al. 2018, Paciência et al., Paciência et al. 2016).

7. One paper reported exposure in hospitals (Fan et al. 2021).

8. Some papers such as Campagnolo et al. (2017) specifically focussed on VOCs, whereas others such as Datta et al. (2017) included VOCs in a review of indoor air quality hence may be of less relevance.

Papers

- Adebayo, O. J., O. O. Abosede, F. B. Sunday, A. A. Ayooluwa, A. J. Adetayo, S. J. Ademola & A. F. Alaba (2018) Indoor air quality level of total volatile organic compounds (TVOCs) in a university offices. *International Journal of Civil Engineering and Technology*, 9, 2872-2882.
- Alomirah, H. F. & H. M. Moda (2020) Assessment of indoor air quality and users perception of a renovated office building in manchester. *International Journal of Environmental Research and Public Health*, 17.
- Cacho, C., G. Ventura Silva, A. O. Martins, E. O. Fernandes, D. E. Saraga, C. Dimitroulopoulou, J. G. Bartzis, D. Rembges, J. Barrero-Moreno & D. Kotzias (2013) Air pollutants in office environments and emissions from electronic equipment: A review. *Fresenius Environmental Bulletin*, 22, 2488-2497.
- Campagnolo, D., D. E. Saraga, A. Cattaneo, A. Spinazzè, C. Mandin, R. Mabilia, E. Perreca, I. Sakellaris, N. Canha, V. G. Mihucz, T. Szigeti, G. Ventura, J. Madureira, E. de Oliveira Fernandes, Y. de Kluizenaar, E. Cornelissen, O. Hänninen, P. Carrer, P. Wolkoff, D. M. Cavallo & J. G. Bartzis (2017) VOCs and aldehydes source identification in European office buildings - The OFFICAIR study. *Building and Environment,* 115, 18-24.
- Cometto-Muñiz, J. E. & M. H. Abraham (2015) Compilation and analysis of types and concentrations of airborne chemicals measured in various indoor and outdoor human environments. *Chemosphere*, 127, 70-86.
- Datta, A., R. Suresh, A. Gupta, D. Singh & P. Kulshrestha (2017) Indoor air quality of non-residential urban buildings in Delhi, India. *International Journal of Sustainable Built Environment*, 6, 412-420.

- Fahad Alomirah, H. & H. M. Moda (2020) Assessment of Indoor Air Quality and Users Perception of a Renovated Office Building in Manchester. *International journal of environmental research and public health*, 17, 1972. doi: 10.3390/ijerph17061972.
- Fan, J., H. Fan, Z. X. Shen, W. P. Dang, W. Zheng, Z. H. Wang & Y. Fu (2021) Concentration Analysis and Health Risk Assessment of Air Pollutants in Newly Decorated Public Places in Xi'an. *Huan jing ke xue= Huanjing kexue*, 42, 2153-2158.
- Faria, T., M. Almeida-Silva, A. Dias & S. M. Almeida (2016) Indoor air quality in urban office buildings. *International Journal of Environmental Technology and Management,* 19, 236-256.
- Gaur, M., K. Bhandari & A. Shukla (2018) Monitoring of total volatile organic compounds and particulate matter in an indoor environment. *Current science*, 115, 1787-1792.
- Goodman, N., A. Steinemann, A. Wheeler & P. Paevere. Indoor volatile organic compounds in Australia.
- Goodman, N. B., A. J. Wheeler, P. J. Paevere, P. W. Selleck, M. Cheng & A. Steinemann (2018) Indoor volatile organic compounds at an Australian university. *Building and Environment*, 135, 344-351.
- Hwang, T. & J. T. Kim (2013) Assessment of indoor environmental quality in open-plan offices. *Indoor and Built Environment,* 22, 139-156.
- Ji, W., Z. Liu, C. Liu, C. Wang & X. Li (2021) Characteristics of fine particulate matter and volatile organic compounds in subway station offices in China. *Building and Environment,* 188.
- Kozielska, B., E. Brągoszewska & D. Kaleta (2020) Investigation of indoor air quality in offices and residential homes in an urban area of Poland. *Air Quality, Atmosphere and Health,* 13, 131-141.

- Kozielska, B. & D. Kaleta (2021) Assessment of indoor benzene and its alkyl derivatives concentrations in offices belonging to university of technology (Poland). *Atmosphere*, 12.
- Kraus, M. & I. J. Šenitková. Level of Total Volatile Organic Compounds (TVOC) in the context of Indoor Air Quality (IAQ) in Office Buildings.
- Licina, D. & S. Langer (2021) Indoor air quality investigation before and after relocation to WELL-certified office buildings. *Building and Environment,* 204.
- Lu, C. Y., J. M. Lin, Y. Y. Chen & Y. C. Chen (2015) Building-related symptoms among office employees associated with indoor carbon dioxide and total volatile organic compounds. *International Journal of Environmental Research and Public Health*, 12, 5833-5845.
- Lucattini, L., G. Poma, A. Covaci, J. de Boer, M. H. Lamoree & P. E. G. Leonards (2018) A review of semi-volatile organic compounds (SVOCs) in the indoor environment: occurrence in consumer products, indoor air and dust. *Chemosphere*, 201, 466-482.
- Mandin, C., M. Trantallidi, A. Cattaneo, N. Canha, V. G. Mihucz, T. Szigeti, R. Mabilia, E. Perreca, A. Spinazzè, S. Fossati, Y. De Kluizenaar, E. Cornelissen, I. Sakellaris, D. Saraga, O. Hänninen, E. De Oliveira Fernandes, G. Ventura, P. Wolkoff, P. Carrer & J. Bartzis (2017) Assessment of indoor air quality in office buildings across Europe The OFFICAIR study. *Science of the Total Environment*, 579, 169-178.
- Mokalled, T., J. Adjizian Gérard, M. Abboud, C. Liaud, R. Nassreddine & S. Le Calvé (2019) An assessment of indoor air quality in the maintenance room at Beirut-Rafic Hariri International Airport. *Atmospheric Pollution Research,* 10, 701-711.

- Paciência, I., J. Madureira, J. Cavaleiro Rufo, E. Oliveira Fernandes, A. Moreira & J. P. Teixeira. Trends of volatile organic compounds in different indoor microenvironments: A review. 7-10.
- Paciência, I., J. Madureira, J. Rufo, A. Moreira & E. O. Fernandes (2016) A systematic review of evidence and implications of spatial and seasonal variations of volatile organic compounds (VOC) in indoor human environments. *Journal of Toxicology and Environmental Health* - *Part B: Critical Reviews*, 19, 47-64.
- Saidin, H., A. A. Razak, M. F. Mohammad & A. Z. U. S. M. Japeri.
 Investigation of indoor air quality in bank offices.
- Sakellaris, I., D. Saraga, C. Mandin, Y. de Kluizenaar, S. Fossati, A. Spinazzè, A. Cattaneo, V. Mihucz, T. Szigeti, E. de Oliveira Fernandes, K. Kalimeri, R. Mabilia, P. Carrer & J. Bartzis (2021) Association of subjective health symptoms with indoor air quality in European office buildings: The OFFICAIR project. *Indoor air*, 31, 426-439.
- Sakellaris, I. A., E. I. Tolis, D. E. Saraga & J. G. Bartzis (2017) VOCS, PAHS and IONS measurements in an office environment in the vicinity of a small industry. *Fresenius Environmental Bulletin*, 26, 292-300.
- Sasic Kalagasidis, A., F. Domhagen & S. Langer. Early-stage concentrations of formaldehydes and TVOCs in a new low-energy building.
- Sérafin, G., P. Blondeau & C. Mandin. Indoor air pollutant screening in office buildings: A differentiated risk approach.
- Spinazzè, A., D. Campagnolo, A. Cattaneo, P. Urso, I. A. Sakellaris, D. E. Saraga, C. Mandin, N. Canha, R. Mabilia, E. Perreca, V. G. Mihucz, T. Szigeti, G. Ventura, E. de Oliveira Fernandes, Y. de Kluizenaar, E. Cornelissen, O. Hänninen, P. Carrer, P. Wolkoff, D. M. Cavallo & J. G. Bartzis (2020) Indoor gaseous air pollutants determinants in office buildings—The OFFICAIR project. *Indoor air,* 30, 76-87.

- Vilcekova, S. & Z. Budaiova. Productivity and indoor environmental quality in offices. 993-1000.
- Wang, S., H. Sadatsafavi, T. Larson & A. Kim. Characterization of indoor air quality in a government office building using principal component analysis.

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