Meeting

Statement on aircraft cabin air quality – First Draft

This is a paper for discussion.

This does not represent the views of the Committee and should not be cited.

Introduction

1. The COT has been asked by DfT to investigate if any new data have been published and to re-evaluate their previous view in the original statement from 2007 (COT, 2007) and position statement from 2013 (COT, 2013). The COT reviewed an introductory paper on this topic on cabin air in May 2022 (TOX/2022/30), which provided a full background to the Committee's previous conclusions. Following the May 2022 COT meeting, the request of COT was further refined to: "Is there evidence of exposure to chemical contaminants in cabin air that could have long-term health impacts, either from acute exposures or due to long-term low level exposures including mixtures, e.g., of volatile organic compounds (VOCs)?".

2. A number of papers presenting data on the concentrations of chemicals in cabin air have been discussed by COT members between May 2022 and March 2023.

3. At the COT meeting in March 2023, it was agreed to produce a draft statement concerning the conclusions drawn by members based on the papers presented. The first draft statement is attached as Annex 1 to this paper.

4. Also at the March 2023 meeting, the Committee agreed that a hazard index (HI) approach should be used to provide an initial screen on the potential for mixture effects from VOCs. This has been undertaken and further detail provided below, along with insertion of initial text on the topic in the draft statement (see para 20-21 in Annex 1).

Hazard Index approach for assessment of mixtures of VOCs

5. In the March 2023 meeting, Members discussed how to assess the potential for mixture effects of VOCs and agreed an initial screening approach should be carried out by calculating hazard quotients (HQ) for the six VOCs that were higher in aircraft cabin air compared with other modes of transport or other work environments, and consequently the HI (Table 1). A HQ is the ratio of the potential exposure to a substance and the level at which no adverse effects are expected i.e., the chronic derived no effect level (DNEL), and the HI is the sum of the HQ for substances that affect the same target organ or tissue. A HI value of less than 1 indicates that no effects, including mixture effects, would be expected. When the HI value is 1 or above, further consideration should be made of any potential mixture risk, e.g. investigate whether the substances have a common or linked mode of action (EA, 2022).

6. For each chemical, inhalation DNELs for workers based on systemic effects following long-term exposure were collated to calculate the HI. Members noted that this approach would be precautionary as the DNELs were based on different effects, and not related to neurological endpoints, which would be most relevant to the symptoms reported.

7. There is no DNEL derived for hexanoic acid. Therefore, a provisional DNEL has been calculated in accordance with ECHA R.8 guidance (ECHA, 2012). A no observed adverse effect level (NOAEL) of 1000 mg/kg bw/day (highest dose tested) obtained from a 28-day oral study in Wistar rats and an oral Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test in Sprague Dawley rats (Potokar, 1983 and Nagao et al. 2002 cited in the REACH dossier for hexanoic acid, respectively) was selected as the basis of the DNEL. The NOAELs were the highest dose tested as no adverse effects were observed. The oral NOAEL was converted to the corresponding air concentration in workers (0.38 m^3/kg for 8 hours exposure of workers) and corrected for the difference between basal caloric demand and caloric demand under light activity (6.7 m^3/10m^3) to give a rounded no observed adverse effect concentration (NOAEC) of 1800 mg/m^3. A total uncertainty factor of 60 (10 for intra-species differences and 6 for use of a sub-acute study) was applied to the NOAEC to give a DNEL of 30 mg/m^3 (30,000 µg/m^3).

Table 1. HQ calculation for six VOCs

VOC	Highest mean conc. in aircraft ($\mu g/m^3$)	DNEL ($\mu g/m^3$)	Endpoint	HQ
1,2-Propanediol	45.2	168000	Decreased body weight	0.0003
2-Phenoxyethanol	4.6	5700	OEL	0.0008
Decanal	14.0	24860	No effect at highest dose	0.0006
Ethanol	386.0	380000	Carcinogenicity	0.0010
Hexanoic acid	6.2	30000*	No hazard identified	0.00021
Octanal	4.2	1300	Decreased liver and kidney weight	0.0032
HI	n/a	n/a	n/a	0.0061

*There is no DNEL derived for hexanoic acid hence a provisional DNEL has been calculated.

8. Based on the HQs presented in Table 1, the HI is 0.0061. As the HI is less than 1, no effects, including mixture effects, would be expected.

Questions for the Committee

9. The Committee is asked to consider:

i. Does the Committee have any comments on the general structure and content of this draft statement?

ii. Does the Committee have any comments about the Hazard Index for mixtures of six VOCs?

iii. Is the Committee content with its conclusions presented within this draft statement?

iv. Does the Committee have any other comments on this draft statement?

IEH-C under contract supporting the UKHSA COT Secretariat

July 2023

TOX/2023/36 Annex 1

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July 2023

Background and scope of review

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). Subsequently in 2013, the COT reviewed the results of DfT-funded aircraft cabin environment research commissioned in response to recommendations made by COT in 2007 and published a position statement (COT, 2013).

2. The COT has now been asked by DfT to investigate if any new data have been published and to re-evaluate their previous view in the original statement from 2007 (COT, 2007) and position statement from 2013 (COT, 2013). Following the May 2022 COT meeting, in which an introductory paper on cabin air was presented (TOX/2022/30), the request of COT was further refined to: “Is there evidence of exposure to chemical contaminants in cabin air that could have long-term health impacts, either from acute exposures or due to long-term low level

exposures including mixtures, e.g., of volatile organic compounds (VOCs)?".

Previous opinions

3. In the 2007 statement, the COT 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).

4. To address recommendations made by COT, DfT commissioned four studies that 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. In 2013, COT reviewed a discussion paper on exposure monitoring of the aircraft cabin environment, covering the four projects commissioned by DfT; 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); and produced a position paper on cabin air (COT, 2013). The Committee came to a number of conclusions including:

- "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.
- "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.
- "The Committee considers that a toxic mechanism for the illness that has been reported in temporal relation to fume incidents is unlikely.
- "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" (COT, 2013).

Current COT review

5. The COT have again been asked by DfT to review any new data that have been published and to re-evaluate their previous views set out in the original statement (COT, 2007) and the position statement (COT, 2013). The Committee reviewed a number of topics related to cabin air quality. Members considered an introductory paper on cabin air in May 2022 (TOX/2022/30), which provided a full background to the Committee's previous conclusions. An updated search of the literature related to the potential health risks from OP exposure in aircraft cabin air was presented to the Committee in July 2022 (TOX/2022/40). Papers on VOCs and sVOCs in aircraft compared with other modes of transport (TOX/2022/46) and work environments (TOX/2022/55) were presented at the September 2022 and October 2022 meetings, respectively. Subsequently, VOCs in European aircraft cabin air were specifically assessed and compared with various regulatory standards such as occupational standards, indoor air quality guidelines and health-based guidance values in March 2023 (TOX/2023/15). Following the Committees' discussions in September 2022, a paper was considered specifically covering carbon monoxide (CO) and carbon dioxide (CO2) (TOX/2022/65) was discussed in December 2022. Further work was then carried out to understand the basis of the regulatory values for carbon dioxide in air (TOX/2023/14) in March 2023. A list of all discussion papers considered by the COT during the review is given in Annex A.

6. The format of discussion papers included systematic reviews, short data summaries, and follow-on papers focussing on specific aspects raised during more in-depth discussions. The evidence base was identified as described in the individual discussion papers.

7. The main aspects of the data presented in these papers and the conclusions drawn by the Committee are summarised in subsequent sections of this statement. The reader is referred to the links to individual discussion papers throughout the text for additional background information.

Organophosphates in aircraft cabin air

8. The potential risk to health from OP exposure in cabin air was discussed in TOX/2022/40. A literature search was carried out using the original search

terms and inclusion and exclusion criteria, focussing on literature published between 2013 and 2021.

9. A number of papers were identified and either presented primary data or an overview of data relating to OPs and adverse health effects in air crew and included an associated risk assessment for the OP tri-ortho-cresyl phosphate (ToCP).

10. For the two epidemiological studies identified, the COT considered there were shortcomings with both studies, in particular in terms of the lack of measured data on OP exposure. Despite this, the COT agreed with the authors conclusions that did not indicate an association between observed cognitive impairment and proxy measures of OP exposures.

11. One paper carried out a risk assessment of tricresyl phosphate (TCP) in aircraft. Members disagreed with some conservative assumptions made in the derivation of the acceptable daily intake but noted that the exposure was substantially lower (2500 times lower) than the derived acceptable intake.

12. Based on the literature found on OPs, the Committee concluded that the adverse effects reported by cabin crew were unlikely to be due to exposure to triaryl phosphates (or other organophosphates) in aircraft cabin, due to the low levels measured.

13. This is in agreement with the conclusion from the COT 2007/06 statement which stated ‘it was not possible……to conclude that there is a causal association between cabin air exposures (either general or following incidents) and ill-health in commercial aircraft crews’ (COT, 2007) and the position paper from 2013, that concluded ‘the Committee considers that a toxic mechanism for the illness that has been reported in temporal relation to fume incidents is unlikely’ (COT, 2013).

VOCs in aircraft cabin air

14. The potential risks from VOCs present in cabin air was considered across a number of papers. The approach adopted focussed on considering whether exposures in aircraft were higher than in other environments, and then, where necessary, considering a risk assessment of those substances where aircraft have the highest concentrations.

15. A literature search was initially carried out to collate concentrations of VOCs in aircraft flying worldwide. Such levels were compared against those reported in other modes of transport including cars and taxis, buses and metros (TOX/2022/46) and other work environments such as offices, schools and hospitals (TOX/2022/55) worldwide, to support consideration of whether exposures to VOCs in aircraft flying worldwide are different to exposures elsewhere. Members agreed that data from the two papers should be reassessed to focus on data from UK and EU-operated aircraft in comparison with data on UK and EU modes of transport and work environments, as they flagged the variability in regulations and weather conditions, amongst other factors, on VOC concentrations around the world. These data were presented in TOX/2023/15 and were, where possible, compared to workplace standards, indoor air quality guidelines or health-based guideline values. It was agreed that any VOCs not exceeding such values would be of low priority for risk assessment.

16. When comparing VOCs in aircraft with other modes of transport, Members noted that data represented a range of vehicle types, usage patterns and sample numbers, all of which affected the comparability of the data across the various modes of transport and even from study to study. Differences in the duration of time generally spent in different vehicle types (e.g., aeroplanes compared to cars) were also noted.

17. In comparing data for UK and EU-operated aircraft and UK and EU modes of transport and work environments, the highest mean concentrations of 1,2-propanediol, 2-phenoxyethanol, decanal, ethanol, hexanoic acid and octanal reported in aircraft were above the highest reported mean concentrations for other modes of transport or work environments (TOX/2023/15). For all other VOCs for which data were available, there was at least one mode of transport or work environment where the highest mean concentration was above the highest mean concentration reported in aircraft.

18. These highest mean concentrations of 1,2-propanediol, 2-phenoxyethanol, decanal, ethanol, hexanoic acid and octanal were compared against UK EH40 occupational standards (HSE, 2020), Public Health England (PHE) indoor air quality guidelines (IAQ) (PHE, 2019) as well as European chronic and acute derived no effect levels (DNELs) for workers via inhalation exposure, as cited in REACH dossiers[1]. The concentrations of all chemicals were below UK occupational standards, PHE IAQs and EU REACH acute and chronic DNELs, indicating that no risk to health is anticipated.

Potential for effects of mixtures of VOCs

19. As the request to the COT included considering the potential for mixture effects of VOCs, the Committee agreed an initial screening approach should be carried out by calculating hazard quotients (HQ) for the six VOCs identified, for which the highest mean concentrations in aircraft were higher than any other modes of transport or work environments and determining the Hazard Index (HI) (Table 1). A HQ is the ratio of the potential exposure to a substance and a health-based guidance level or level at which no adverse effects are expected, and the HI is the sum of the HQ for the individual substances. A HI value of less than 1 indicates that no effects, including mixture effects, would be expected. When the HI value is 1 or above, further consideration should be made of any potential mixture risk, e.g. investigate whether the substances have a common or linked mode of action (EA, 2022). In this instance, the highest mean concentration was compared with the published chronic inhalation DNEL for workers based on systemic effects after long-term exposure for each substance, with the exception of hexanoic acid as no DNEL was available. Instead, for hexanoic acid a provisional DNEL has been calculated in accordance with ECHA R.8 guidance (ECHA, 2012). A no observed adverse effect level (NOAEL) of 1000 mg/kg bw/day (highest dose tested) obtained from a 28-day oral study in Wistar rats and an oral Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test in Sprague Dawley rats (Potokar, 1983 and Nagao et al. 2002 cited in the REACH dossier for hexanoic acid, respectively) was selected as the basis of the DNEL. The NOAELs were the highest dose tested as no adverse effects were observed. The oral NOAEL was converted to the corresponding air concentration in workers (0.38 m^3/kg for 8 hours exposure of workers) and corrected for the difference between basal caloric demand and caloric demand under light activity (6.7 m^3/10m^3) to give a no observed adverse effect concentration (NOAEC) of 1800 mg/m^3. A total uncertainty factor of 60 (10 for intra-species differences and 6 for use of a sub-acute study) was applied to the NOAEC to give a DNEL of 30 mg/m^3 (30,000 µg/m^3).

20. The Committee considered that the HI approach would be precautionary as the DNELs were based on different effects, and not related to neurological endpoints.

Table 1. HQ and HI calculation for six VOCs

VOC	Highest mean conc. in aircraft (µg/m^3)	DNEL (µg/m^3)	Endpoint	HQ
1,2-Propanediol	45.2	168000	Decreased body weight	0.0003
2-Phenoxyethanol	4.6	5700	OEL	0.0008
Decanal	14.0	24860	No effect at highest dose	0.0006
Ethanol	386.0	380000	Carcinogenicity	0.0010
Hexanoic acid	6.2	30000*	No hazard identified	0.0021
Octanal	4.2	1300	Decreased liver and kidney weight	0.0032
HI	n/a	n/a	n/a	0.0061

*There is no DNEL derived for hexanoic acid hence a provisional DNEL has been calculated.

21. Based on the HQs presented in Table 1, the calculated HI is 0.0061. As the HI is less than 1, no effects, including mixture effects, would be expected.

CO and CO2 in aircraft cabin air

22. Levels of CO2 and CO in UK and EU-operated aircraft were collated and compared with regulatory values in aircraft, workplace exposure standards and air quality standards, as well as levels that cause adverse health effects (TOX/2022/65).

23. For CO, no mean data were available for EU and UK flights, but the maximum concentration (4.8 ppm) was below all regulatory values for aircraft (50 ppm) and air quality standards (8.6-87 ppm), with the exception of the World Health Organisation (WHO) Air Quality Guideline (AQG) of 4 mg/m^3 (3.4 ppm) (WHO, 2021). The maximum concentration of CO was also below levels that are reported to cause adverse health effects (70-350 ppm) (Higgins et al., 2005). The Committee concluded that levels of CO in aircraft are unlikely to be associated with ill health.

24. The highest mean concentration of CO2 reported in UK and EU-operated aircraft was 1417 ppm and the maximum concentration was 2771 ppm (TOX/2022/65). These levels are lower than the Certification Specifications (CS) aircraft standard and workplace exposure limits (WELs; 5000 ppm) and concentrations that were associated with no noticeable symptoms (5500 ppm for 6 hours) (Safe Work Australia, 2019).

25. However, the maximum reported concentrations exceed guideline concentrations indicating poor indoor air quality in residential and non-residential buildings, where CO2 is used as a marker of indoor air quality. The highest mean concentration is in the range of medium or acceptable indoor air quality guideline concentrations (Lowther et al., 2021).

26. The Committee agreed that effects of CO2 should be assessed in terms of acute and chronic exposure as adverse effects may be different. Measured concentrations were higher than those reported in some epidemiological studies of indoor environments to cause acute transient effects such as decreased cognition and increased heart rate, though these findings were not replicated in other studies often in laboratory or controlled settings (Lowther et al., 2021). The Committee recognised that such effects could be of concern as they may impact on decision making in aircraft crew, however in reviewing the evidence base, the Committee did not consider these endpoints to directly occur as a result of exposure to CO2. There was considered to be potential for the effects to be secondary to physiological effects related to acid-base balance in the body and respiratory drive at higher concentrations of CO2, though the Committee considered that people exposed to such concentrations of CO2 would be aware of the resultant physiological effects.

27. Following low level chronic exposure, there was little evidence available for adverse effects.

28. Overall, it was concluded that exposure to CO2 was unlikely to cause symptoms that are not attributable to the physiological effects of CO2.

Discussion

29. Following a request by DfT to assess if any new data have been published to address if chemical contaminants in cabin air could have long term health impacts, a number of papers have been considered by the COT (Annex A).

30. As previously, the Committee recognised the reports of ill health and symptoms, in relation to aircraft cabin air. The Committee also considered that it was important, regardless of the whether a causal link can be identified, for actions to continue to minimise the risk of fume incidents giving risk to symptoms.

31. From the literature found on OPs, the Committee concluded it was unlikely that the adverse effects reported by cabin crew were due to exposure to organophosphates in aircraft cabin air.

32. The Committee considered that although concentrations of six VOCs were higher in UK and EU-operated aircraft compared with other modes of transport and work environments in UK and EU, concentrations were below UK occupational standards, PHE IAQs and EU REACH acute and chronic DNELs, indicating that negligible risk to health is anticipated. Moreover, using a HI approach, exposure to the mixture of such VOCs in aircraft cabin air did not indicate a concern for potential mixture risk.

33. Regarding CO, the Committee concluded that concentrations in aircraft are unlikely to be associated with ill health.

34. For CO2, the Committee recognised that decreased cognition and increased heart rate reported in some epidemiology studies of indoor environments, though these findings were not replicated in other studies with more controlled environments. Such effects could be of concern as they may impact on decision making in aircraft crew, however, the Committee did not consider these endpoints to directly occur as a result of exposure to CO2 but as a secondary outcome to physiological effects at higher concentrations of CO2. Following low level chronic exposure, there was little evidence available for adverse effects. Overall, the Committee concluded that exposure to CO2 was unlikely to cause symptoms that are not attributable to the physiological effects of CO2.

35. The COT notes that a number of factors could potentially confound a possible association between the symptoms reported with chemicals in the aircraft cabin air environment, including temperature, humidity, ventilation, human bioeffluents, stress, circadian rhythm, radiation exposure and shift work. Such confounders are outside the COT remit to evaluate.

36. These conclusions made by the Committee are in agreement with conclusions from previous statements and position papers that state 'it was not possible……to conclude that there is a causal association between cabin air exposures (either general or following incidents) and ill-health in commercial aircraft crews' (COT, 2007) and 'the Committee considers that a toxic mechanism for the illness that has been reported in temporal relation to fume incidents is unlikely' (COT, 2013).

Overall conclusion

37. The COT has been asked by DfT to investigate if any new data have been published and to re-evaluate their previous view in the original statement from 2007 (COT, 2007) and position statement from 2013 (COT, 2013) regarding the cabin air environment, and to expand the review to cover exposure to VOCs within aircraft. Following the May 2022 COT meeting, the request of COT was further refined to: "Is there evidence of exposure to chemical contaminants in cabin air that could have long-term health impacts, either from acute exposures or due to long-term low level exposures including mixtures, e.g., of volatile organic compounds (VOCs)?".

38. Based on the data collated, in line with conclusions from the COT 2007/06 statement (COT, 2007) and the position paper from 2013 (COT, 2013), the Committee concluded that there is no evidence that exposure to chemical contaminants (OPs, VOCs including as mixtures, CO and CO2) in aircraft cabin air are likely to be associated with ill health of commercial airline crews following acute or long-term low level exposures.

COT

Date; Statement 20XX/XX

Acknowledgements

Brian Roberts, Civil Aviation Authority

Abbreviations

AQG	Air Quality Guideline
ASHRAE	American Society of Heating, Refrigerating and Air-Conditioning Engineer
BALPA	British Airline Pilots Association
COT	Committee on Toxicity
CO	Carbon monoxide
CO2	Carbon dioxide
CS	Certification Specifications
DfT	Department for Transport
DNEL	Derived no effect level
HI	Hazard index
HQ	Hazard quotient
HSE	Health and Safety Executive
IAQ	Indoor air quality
NOAEC	No observed adverse effect concentration

NOAEL	No observed adverse effect level
PHE	Public Health England (now UK Health Security Agency (UKHSA))
sVOC	Semi-volatile organic compound
TDI	Tolerable daily intake
TCP	Tricresyl phosphate
ToCP	Tri- ortho-cresyl phosphate
TWA	Time weighted average
UF	Uncertainty factor
VOC	Volatile organic compound
WEL	Workplace exposure limit
WHO	World Health Organisation

References

EA, 2022. Evaluation of the potential appraoched to risk assessment of unintentional chemical mixtures for future UK REACH assessments. Environment Agency, Bristol.

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. cotstatementbalpa200706.pdf (nationalarchives.gov.uk)

COT, 2013. Discussion paper on exposure monitoring of the aircraft cabin environment. TOX/2013/32. tox201332.pdf (food.gov.uk)

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. Acetylcholinesterase and neuropathy target esterase activities in 11 cases of symptomatic flight crew members after fume events - PubMed (nih.gov)

ECHA (2012). Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health. ECHA. Guidance on Information Requirements and Chemical Safety Assessment - ECHA (europa.eu)

ECHA (2022). REACH dossier for hexanoic acid. Registration Dossier - ECHA (europa.eu)

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.

Higgins, C. (2005). Causes and clinical significance of increased carboxyhemoglobin. Causes and clinical significance of increased carboxyhemoglobin (acutecaretesting.org)

HSE. (2020). EH40/2005 Workplace exposure limits. EH40/2005 Workplace exposure limits (hse.gov.uk)

Lowther, S.D., Dimitroulopoulo, A., Foxall, K., Shrubsole, C., Cheek, E., Gadeberg, B., & Sepai, O. (2021). Low level carbon dioxide indoors - a pollution indicator or a pollutantt? A health-based perspective. Perspective. Environments, 8, 125. https://doi.org/10.3390/environments8110125

IGHRC (2009). Chemical Mixtures: A framework for assessing risks to human health (CR14). Institute of Environment and Health, Cranfield University, UK. Chemical Mixtures: A framework for assessing risks to human health (iehconsulting.co.uk)

PHE (2019). Indoor Air Quality Guidelines for selected Volatile Organic Compounds (VOCs) in the UK. Air quality: UK guidelines for volatile organic compounds in indoor spaces - GOV.UK (www.gov.uk)

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. Cognitive impairment and associated loss in brain white microstructure in aircrew members exposed to engine oil fumes - PMC (nih.gov)

Safe Work Australia (2019). Draft evaluation report - Carbon dioxide. draft-evaluation-report-wes-carbon-dioxide-pdf.pdf (amazonaws.com)

WHO (2021). WHO global air quality guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. ADDIN EN.REFLIST WHO global air quality guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide

Annex A

The following papers have been presented to the COT:

May 2022 – Introductory scoping paper (TOX/2022/30): Blank style sheet for COT Papers 2014 (food.gov.uk)

July 2022 – updated literature on potential health risks from organophosphate exposure in aircraft cabin air (TOX/2022/40): Blank style sheet for COT Papers 2014 (food.gov.uk)

September 2022 – Presentation from Civil Aviation Authority on data analysis of reports, engine seals, operator actions and future developments/modifications.

September 2022 – Volatile organic compounds in aircraft cabin air: comparison with other modes of transport (TOX/2022/46): Blank style sheet for COT Papers 2014 (food.gov.uk)

October 2022 – Volatile organic compounds in aircraft cabin air: comparison with work environments (TOX/2022/55): Blank style sheet for COT Papers 2014 (food.gov.uk)

December 2022 – Carbon monoxide and carbon dioxide in aircraft cabin air (TOX/2022/65): Aircraft Cabin Air - CO2 and CO (food.gov.uk)

March 2023 – Aircraft cabin air: Basis of the regulatory values for carbon dioxide (TOX/2023/14): Blank style sheet for COT Papers 2014 (food.gov.uk)

March 2023 – Volatile organic compounds in European aircraft cabin air: concentrations and comparison with regulatory standards (TOX/2023/15): Blank style sheet for COT Papers 2014 (food.gov.uk)

[1] ECHA website: https://echa.europa.eu/