Meeting

Statement on aircraft cabin air quality – Second 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 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. A first draft statement was presented at the COT meeting in July 2023. Following comments from the Committee, a second draft of the statement is attached as Annex 1 to this paper.

Questions for the Committee

3. The Committee is asked to consider:

i. Does the Committee have any further comments on this second draft statement?

IEH-C under contract supporting the UKHSA COT Secretariat

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TOX/2023/48 Annex 1

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).

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

2. 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).

3. 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.
- "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

4. The COT have again been asked by DfT to review any new data that have been published on chemical exposure and possible effects on the health of cabin crew 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 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.

5. 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.

6. 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.

7. The studies presented in all discussion papers reported background exposures to the contaminants under investigation, due to the paucity of data on short-term peaks that may occur during oil or hydraulic fluid smoke or fume contamination incidents in commercial aircraft.

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 the data did not indicate any 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. Even though members felt that some of the assumptions made in the derivation of the acceptable daily intake were too conservative, it was 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 previous COT 2007/06 statement which stated ‘the balance of evidence is not supportive of an association between chronic low level exposure to OPs and neuropsychological deficits in tests or the occurrence of OPICN’ (organophosphate ester induced chronic neurotoxicity) (COT, 2007) and the position paper from 2013, that concluded ‘the pattern 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 o-TCP’ (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, levels of air pollution, 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 (n=37), 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 at these levels.

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 NOAEL was 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), reflecting inter-species difference, 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 conservative as the DNELs were based on different effects, and not related to common 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	-	-	-	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 all of the HQs and the HI are substantially 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 for 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) as a 24-hour mean (WHO, 2021). It was noted that the AQG was based on epidemiological studies on air pollution and as noted by the authors "Ambient carbon monoxide concentrations may be highly correlated with other air pollutants … which may significantly confound the observed risk estimates.” 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. Although the maximum reported concentrations exceed guideline concentrations for air quality in residential and non-residential buildings, it was noted that in this situation CO2 is used as a marker of indoor air quality and the guideline concentration is not associated with adverse effects of CO2 itself on health. 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 both acute and chronic exposure to CO2 should be assessed as the adverse effects would be different. Measured concentrations were lower than those consistently shown to cause acute transient effects such as decreased cognition and increased heart rate (Lowther et al., 2021). However, the Committee recognised that should such effects occur, they could be of concern as they may impact on decision making in aircraft crew, but in reviewing the evidence base, the Committee did not consider the effects occurred directly as a result of exposure to CO2 at the levels reported in aircraft. At higher concentrations of CO2 there was potential for central nervous system (CNS) effects, secondary to physiological effects related to perturbations of the acid-base balance in the body and respiratory drive. The Committee considered that it was likely 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 for any adverse effects.

28. Overall, it was concluded that exposure to CO2, at the levels reported in aircraft, was unlikely to cause any adverse health effects, either acutely or chronically.

Discussion

29. Following a request by DfT to assess whether there is any new evidence that exposure to chemical contaminants in cabin air could have long-term health impacts, either from acute exposures or due to long-term low level exposure including mixtures, e.g. of volatile organic compounds (VOCs), a number of

papers have been considered by the COT (Annex A).

30. From the literature found on OPs, the Committee confirmed its previous conclusion that it was unlikely that the adverse effects reported by cabin crew were due to exposure to organophosphates in aircraft cabin air.

31. The Committee noted that the highest mean concentrations of most VOCs in UK and EU-operated aircraft were lower than those in at least one other mode of transport or work environments in UK and EU. For six other VOCs, although the highest mean concentrations in UK and EU-operated aircraft were above those in other modes of transport and work environments, they were all well below UK occupational standards, PHE IAQs and EU REACH acute and chronic DNELs, indicating that adverse effects on health were unlikely at the exposure levels reported in aircraft. Moreover, using a screening level HI approach, it was concluded that exposure to a mixture of these six VOCs, each present at its maximum mean concentration, in aircraft cabin air, was highly unlikely to have any adverse effects on health.

32. Regarding CO, the Committee concluded that concentrations in aircraft reported were such that they were unlikely to have adverse effects on health.

33. For CO2, the Committee concluded that the concentrations reported in cabin air were all below health-based guidance values and that exposure to CO2 at these levels was unlikely to be associated with adverse effects on health.

34. 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.

Overall conclusion

35. The COT was asked by DfT to investigate whether there is any 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). This was a follow-up to the Committee’s previous statement from 2007 (COT, 2007) and position statement from 2013 (COT, 2013) on chemical exposure and possible effects on the health of cabin crew. It was noted that the terms of reference differed somewhat in that the previous review focused particularly on

concerns about the possible effects on aircrew health of oil or hydraulic fluid smoke or fume contamination incidents in commercial aircraft.

36. The COT concluded that the levels of the chemical contaminants reviewed (OPs, VOCs including as mixtures, CO and CO2) in aircraft cabin air are unlikely to cause adverse health effects in cabin crew following acute or long-term exposures.

37. The Committee noted that most of the published information on chemical concentrations in cabin air were on background levels, and that there continued to be a dearth of information on levels following fume events. Hence, specific measurements of contaminants during real-time monitoring of aircraft could assist in assessing the significance of these events.

38. The Committee did not review the possible etiology of ill health in cabin crew, so while it was possible to reach conclusions on the chemicals reviewed in the scenarios reported, only limited conclusions could be reached on other scenarios and no conclusions could be reached on the possible contribution of other factors, such as temperature, humidity, ventilation, human bioeffluents, stress, circadian rhythm, radiation exposure and shift work.

COT

Date; Statement 20XX/XX

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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

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

Annex A

Statement on aircraft cabin air quality

The following papers have been presented to the COT:

May 2022 – Introductory scoping paper (TOX/2022/30)

July 2022 – updated literature on potential health risks from organophosphate exposure in aircraft cabin air (TOX/2022/40)

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)

October 2022 – Volatile organic compounds in aircraft cabin air: comparison with work environments (TOX/2022/55)

December 2022 – Carbon monoxide and carbon dioxide in aircraft cabin air (TOX/2022/65)

March 2023 – Aircraft cabin air: Basis of the regulatory values for carbon dioxide (TOX/2023/14)

March 2023 – Volatile organic compounds in European aircraft cabin air: concentrations and comparison with regulatory standards (TOX/2023/15)

July 2023 – Statement on aircraft cabin air quality – First Draft (TOX/23/36)

[1] ECHA website: Homepage - ECHA (europa.eu)