Committee on TOXICITY

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD CONSUMER PRODUCTS AND THE ENVIRONMENT

STATEMENT ON THE REVIEW OF THE CABIN AIR ENVIRONMENT, ILL-HEALTH IN AIRCRAFT CREWS AND THE POSSIBLE RELATIONSHIP TO SMOKE/FUME EVENTS IN AIRCRAFT

[This statement is an independent document and the reader is referred to the relevant discussion papers on the website for background information: http://www.advisorybodies.doh.gov.uk/cotnonfood/index.htm]

Introduction

Background to the COT review

1. The COT was asked by the Department for Transport (DfT) to undertake an independent scientific review of data submitted by the British Airline Pilots Association (BALPA) due to concerns about the possible effects on aircrew health of oil/hydraulic fluid smoke/fume contamination incidents in commercial aircraft. BALPA submitted data relating to organophosphate compounds (OPs), the cabin air environment, ill-health in aircraft crews and the possible relationship to smoke/fume events in aircraft. The Department of Health (DH) commissioned the Health Protection Agency (HPA) COT Secretariat and the DH Toxicology Unit, Imperial College London, to review the BALPA submission and prepare discussion papers for the COT.

2. Throughout this document the term air contamination incident is intended to refer to incidents with internal sources (e.g. passengers, aircraft components, cleaning materials, dust, disinsection procedures and contaminants arising from aircraft systems (such as oil in engines). External contamination such as ground level air pollution is not covered in this evaluation.

Overview of BALPA submission

3. BALPA submitted evidence and met with the COT Secretariat in February 2006 (TOX/2006/21 Annex 3) to outline their views in support of their contention that acute and chronic illnesses are being induced in pilots and cabin crew through the inhalation of engine oil and hydraulic fluid, additives present in these products and pyrolysis products that may be emitted from the engines and auxiliary power unit (APU) into the air conditioning system of certain aircraft types during air contamination incidents. BALPA consider that this situation is resulting in significant flight safety issues and has unacceptable implications for the health of flight crew.

BALPA are also concerned that passengers may be suffering similar symptoms to those exhibited by flight crew.

4. BALPA made two submissions of data. The first in June 2005 (denoted as submission A) consisted of 193 references and an additional submission in November 2005 (denoted as submission B) consisted of 73 references. The COT Secretariat obtained documents listed by BALPA as being part of, but absent from, the submission and complete documents where pages were missing from the documents submitted. It was noted that some data and documents were submitted more than once.

5. A large proportion of the references submitted comprised: incident details, summaries of incidents, incident reporting; airline service bulletins/lists of bulletins, statements, information leaflets, communications, messages, air quality standards; oil manufacturers' safety data sheets for oil constituents, and photocopies of oil can labels. Also included were around 60 references relating to OPs, together with a limited number of references relating to oil and hydraulic fluid analysis, neurotoxicity/inhalation toxicity, cabin air quality testing, plus a reference to Gulf War Syndrome, multiple chemical sensitivity and aircraft disinsectants.

6. In addition, the COT Secretariat identified a further 169 relevant references and these are denoted with the prefix 'C'.

7. Although over 400 references have been identified and evaluated only a limited number of key references are quoted in this statement. A number of key references, reviews, evaluations, enquiries and conference reports have been reviewed (references A44, A67, A106, A107, A123, C162, C163) and summaries can be found in TOX/2006/21. The key themes raised in the proceedings of the BALPA air safety and cabin air quality international aero industry conference, Imperial College London, April 2005[A44] (submitted to the COT at its July 2006 meeting) and during a meeting held between the COT Secretariat and BALPA and their nominated representatives, are outlined below:

a. A range of symptoms of ill-health was described by presenters based on assessment of self-reported cases. These included acute/short-term skin, gastrointestinal, respiratory and nervous system symptoms with evidence of long-term respiratory, neurological, chronic fatigue and chemical sensitivity effects reported in some individuals. The term 'aerotoxic syndrome' was cited in the BALPA submission to describe a wide range of acute and chronic symptoms reported by aircrew ostensibly exposed to oil/hydraulic fluid smoke/fume air contamination incidents.[A4] The COT has made a general comment on the value of considering 'aerotoxic syndrome' as a diagnosis under paragraph 28 of this statement.

b. Conference presenters proposed exposure to cresyl phosphates (a type of OP), present in jet oils as anti-wear additives, as potentially responsible for some of the symptoms reported and in particular chronic ill-health. Evidence for exposure to tricresyl phosphate isomers was reported in one limited investigation of air levels in military aircraft but no data were available for commercial jet aircraft. A number of presenters reported clinical examination of pilots and neuropsychological testing that had been undertaken with two BAe 146 pilots. Evidence for neurological impairment was described in one presentation of 26 airline pilots examined clinically and by positron emission tomography (PET) scanning. Reference was made in one presentation to autonomic nervous system symptoms in pilots but no data were presented. One suggestion outlined in the BALPA conference proceedings was that single large doses or repeated small sub-clinical doses of OPs may be associated with neurological, neurobehavioral and neuropsychological consequences referred to as 'organophosphate ester induced chronic neurotoxicity' or OPICN. The COT has commented on the evidence for OPICN in paragraph 59 of this statement.

c. The BALPA conference presenters proposed that there is underreporting to regulators of contamination incidents and associated cases of illness. The COT has commented on this aspect in paragraphs 46 and 48 of this statement.

d. Possible approaches to exposure assessment were described and the practical difficulties of undertaking such investigations on working commercial jet aircraft are noted. One possible approach is the development of a biosensor based on surface plasmon resonance. A proposal for the possible development of such a device was outlined at the meeting with BALPA in February 2006 (TOX/2006/21 Annex 3).

e. Reference was also made at the BALPA conference to the Occupational Health Research Consortium in Aviation (OHRCA) project funded in the US following the publication of the National research Council (NRC) review of aircraft air quality in 2002. The proposal was to recruit 150 flight attendants in Portland and San Francisco and 120 pilots from London to undertake incident reporting and exposure monitoring (using an air sampling device fitted with a pump and filters) in a feasibility study which would then be expanded to involve ongoing monitoring. The COT has commented on possible approaches to further research in paragraphs 64-83 of this statement.

8. Versions of the BALPA database listing alleged smoke/fume incidents recorded by BALPA were submitted to the COT Secretariat on 3 occasions. The submissions were in July 2005, in February 2006 after their meeting with the COT Secretariat and then again in April 2006. The COT Secretariat had commenced analysis of the database submitted in February 2006 when the third version of the database was submitted in April 2006. The February 2006 submission listed 746 reports; the April 2006 submission listed 809 reports and covered the period 1 May 1985 – 4 April 2006. The additional entries were added throughout the database and were not limited to the period February – April 2006 and additional information was provided for some

existing entries. A comparison of the April and February submissions indicated that 13 of the additional entries in the April submission were duplicates of existing entries.

Additional submissions to COT

9. In response to a request from the COT Secretariat for smoke/fume incident data, the Civil Aviation Authority (CAA) submitted the results of two searches for contaminated air events recorded on the Mandatory Occurrence Reporting (MOR) scheme database for the period 1 January 2001 – 4 April 2006. The first search comprised 262 summaries for a range of aircraft types and the second search comprised 99 summaries for the BAe 146 and B757 only. The summaries included details of health symptoms reported by pilots, cabin crew and passengers in addition to details of engineering malfunctions.

10. A short letter was received from BALPA in response to a request from the COT Secretariat for the submission of a number of pilot testimonies.

11. The COT Secretariat received a range of communications from interested parties (including reports of investigations in pilots, letters, emails and telephone calls from individuals and organisations, including campaigners and pressure groups). All information was considered and evaluated for its relevance to the review. Unsolicited information received by the COT Secretariat was also evaluated for its relevance to the submission (reference C164).

12. During the review, the COT received additional submissions of information from a number of independent external specialists including relevant information on approaches to air monitoring for complex mixtures of chemicals in air, the potential evaluation of such mixtures for sensory irritancy, background information on indoor air pollution, risk factors for sensory irritancy, a report of neuropsychological investigations in a number of self-selected pilots, and advice from an expert in aviation medicine on exposure standards for carbon monoxide at the air pressures experienced during commercial flights at high altitude and the potential response of pilots to high altitude flying. (See annexes to COT papers for full details).

13. In March 2007, the COT Secretariat again requested presenters at the BALPA April 2005 conference who had undertaken investigations of pilots to submit any updated data, but no additional information of significance for the review was returned.

14. The COT was aware that the potential exposure of aircrew to oil or hydraulic fluid combustion products is highly controversial within the air industry, and that this independent scientific review of the BALPA submission undertaken by the Committee has generated considerable interest, including some from overseas. As a result, observers attending the meetings have represented a wide range of views and expertise in this area of occupational health.

Advice requested from COT

15. The COT was asked to:

i. Evaluate the BALPA submission and, based on the data submitted by BALPA and that sourced by the COT Secretariat, assess the risk of exposure of aircraft crews to OPs and oil/hydraulic fluid pyrolysis products in cabin air and determine whether there is a case for a relationship between exposure and ill-health in aircraft crews.

ii. Provide the DfT with appropriate advice on any further research required to evaluate this subject.

16. The COT considered a full discussion paper on the referral in TOX/2006/21 at its meeting on 11 July 2006 and updated discussion papers on 5 December 2006 (TOX/2006/39) and 20 March 2007 (TOX/2007/10). A meeting was held with COT epidemiologists and the DH Toxicology Unit on 2 May 2007 to further discuss aspects of health-based research identified at the 20 March 2007 COT meeting. The statement was considered at the 3 July 2007 meeting of the COT.
(http://www.advisorybodies.doh.gov.uk/cotnonfood/index.htm).

Evaluation of BALPA submission

17. The COT discussion paper TOX/2006/21 was structured to review all the information submitted by BALPA in the order presented to the COT Secretariat. A number of topics were identified for further consideration and these related to:

i. Further assessment of incidents, particularly relating to those not reported to airlines or under regulatory schemes such as the CAA MOR scheme.

ii. The development of approaches to measure potential exposure to chemicals during a smoke/fume incident due to oil/hydraulic fluid contamination of the bleed air.

iii. Further assessment of the reported acute and chronic ill-health documented by pilots to include further consideration of the neuropsychological data submitted to the COT on the 11 July 2006, and the blood/fat levels of chemicals in pilots.

iv. A review of all the epidemiological data contained in the BALPA submission and additional data retrieved through literature searches.

v. A full literature search to identify published data not sourced in the BALPA submission or the initial searches undertaken by the COT Secretariat.

18. The COT discussion paper TOX/2006/39 presented information on the topics identified by COT from the July 2006 discussion. Areas for further consideration identified at the December 2006 meeting related to:

i. Further information on whether the pilots making multiple reports of smoke/fume incidents were those who also documented continuing ill-health.

ii. Identification of any further information on exposure to pyrolysed oils and hydraulic fluids.

iii. Possible approaches to investigate further the skill tests/proficiency checks for flight crew licences and ratings in relation to the neuropsychological symptoms documented in a study of self-selected pilots.

19. The COT discussion paper TOX/2007/10 presented information on the topics identified by COT in the December 2006 meeting for further consideration. In addition, a full evaluation of all the epidemiological studies (cross-sectional, case studies, case series) contained in the BALPA submission, together with additional studies retrieved by the COT Secretariat and the DH Toxicology Unit was submitted to the COT (TOX/2007/10 Annex 10).

Description of generic air conditioning system (addendum to TOX/2006/21 annex 5)

20. A brief description of a generic air conditioning system is given below to aid understanding of the physical conditions present during an oil/hydraulic fluid smoke/fume contamination incident. There are a number of differences between commercial aircraft in the design and operation of the air conditioning systems. The BAe 146 and B757 aircraft had generated more reports of contaminated air events than other airframes listed on the BALPA database. Some relevant information regarding the B757 and the BAe 146 is given below.

<u>Bleed air</u>

21. The air supplied to the aircraft air conditioning system is extracted from one or more stages of the aircraft engine compressor and is known as bleed air. The actual temperature and pressure of the air at the extraction point will vary depending on the ambient temperature and pressure, the stage of the compressor used for the extraction, and the speed of the engine. These factors will produce a wide range but the maximum temperature and pressure normally could be about 300-350°C and about 60-80psi (about five times atmospheric pressure) respectively. After being ducted away from the engine, the air is usually immediately cooled to about 200-250°C and controlled to an airframe design pressure in the engine pylon of about 40psi. For the B757, the nominal temperature control is to 177°C ± 17°C /350°F ± 30°F. The

cooled and pressurised air is then ducted into the aircraft and the air conditioning packs where it is further cooled and conditioned.

22. In addition to the engines, the APU on the aircraft provides bleed air for use on the ground and, for some aircraft, in flight, usually until just after take-off and from shortly before landing. Again, the actual temperature and pressure of the air supplied will be dependent on ambient conditions and the running condition of the APU. For the B757, the APU temperatures are nominally 177°C/350°F as there is no precooler present in the APU system, and for the BAe 146 aircraft 200-230°C.

<u>Aircraft air distribution system</u>

23. The conditioned air from the air conditioning packs and the recirculation air are ducted into a mix manifold to ensure uniform temperature. Separate supplies are then drawn for each temperature-controlled zone in the aircraft. Generally, the packs will regulate to the lowest demand and each zone supply then receives a small additional flow of hot bleed ‘trim’ air, extracted from upstream of the pack, to control the main supply to each zone to the appropriate temperature.

24. Most modern aircraft have recirculation systems. The cabin air volume is generally composed of 45% conditioned bleed air with 55% recirculation air.[A107] Air is drawn from the passenger cabin and ducted through filters, generally High Efficiency Particulate Air (HEPA) standard, to remove particulates. It is then blown by fans into the mix manifold downstream of the packs before the individual zone supplies are divided. Typically, air in the cabin will circulate for 2-3 minutes before being exhausted from the aircraft. In the cockpit, the air will be exchanged approximately every minute.[A107] Some aircraft systems exclude recirculated air from the flight deck air supply (e.g. B757) whilst others do not (e.g. BAe 146). Where the exclusion of recirculated air applies, the flight deck supply is extracted upstream of the mix manifold so that it comes from only one pack. In this case, the packs may run at different outlet temperatures depending on the flight deck demand. Air filtration is not required by airworthiness requirements and some aircraft, including the BAe 146, have no filtration in the recirculated air system.

25. The temperature, pressure and humidity of the air will vary between different designs and aircraft types in the air distribution system stages. Typical cabin air temperature is 22°C with a relative humidity of 10-20%.[A107] Humidity within the cabin is predominantly related to the number of people in the aircraft for that flight and is not controlled like cabin temperature and pressure. The overall range of conditions provided by the aircraft and engine systems are similar between different commercial aircraft.

Smoke/fume air contamination incidents

26. An oil/hydraulic fluid smoke/fume air contamination incident is an event in which a small quantity of oil/hydraulic fluid released into the compressor stage of the engine, due to an oil seal failure, is extracted into the bleed air

supplying the aircraft air conditioning system resulting in the formation of an oil mist or odour in the aircraft. The leaked oil/hydraulic fluid is subject to a range of temperatures within the engine and aircraft air conditioning system that might cause thermal decomposition of the oil/hydraulic fluid. Not all odours detected within the aircraft cabin originate from oil contamination of the air supply, for example, toilet and galley odours also occur, and it is not possible to define the cause of all smoke/fume air contamination incidents. It has been estimated from information provided by three airlines that overall, smoke/fume incidents associated with possible explanatory faults identified by engineers (engineering-confirmed smoke/fume incidents) occur in around 0.05% of flights (sectors) but that the incidence may be higher than this in some circumstances, depending on airframe, engine type and servicing (TOX/2006/39 Annexes 13, 14 and 18).

General comments on evidence reviewed

27. The COT recognises that any matter relating to aircrew health must be taken very seriously, both for the protection of the individuals and also to ensure the safe operation of the aircraft.

28. The COT considered as a general point prior to detailed evaluation of the submitted evidence that regardless of the cause(s) of the reported adverse symptoms, it would be prudent to take appropriate action to prevent oil or hydraulic fluid smoke/fume contamination incidents. It was noted that potential irritants may be released during oil or hydraulic fluid contamination incidents and, although on currently available evidence it was not possible to define a chemical or chemical mixtures responsible for the reported acute effects on the skin and respiratory tract, it was reasonable to consider a possible chemical causation in some instances. It was agreed that, while the term 'aerotoxic syndrome' as identified in the BALPA submission was unhelpful because the health problems described were variable between subjects, potentially multi-factorial and also not specific to this situation, it was important that the COT assessed the evidence for any harm resulting from exposure.

COT review of BALPA submission and data sourced by the COT Secretariat

Laboratory investigations of the pyrolysis of jet oils and hydraulic fluids

29. The COT has evaluated the limited number of published laboratory studies of oil pyrolysis. The thermal degradation of jet oils has been shown to form a diversity of volatile organic compounds (VOCs) including ketones, acids, aldehydes, esters, oxygen containing heterocyclic compounds, and tricresyl phosphate isomers (but not the ortho- isomer) in addition to carbon monoxide, carbon dioxide and ozone (TOX/2006/39 Annexes 10, 11 and 12). Some acids are noted to have unpleasant odours (valeric acid, isovaleric acid and caprylic acids) and some potentially irritating aldehydes can be formed (TOX/2006/39 Annex 11). It is noted that the carbon chain length of acid substituents in esters may affect the contaminants formed, and that a higher

proportion of C5 or C6 acids will generally give rise to decomposition products of a higher odour. It is evident that parameters other than amount of oil released into an engine, such as bleed air temperatures and pressures in compression chambers and airflows, would also have an impact on the chemical contaminants formed during an oil/hydraulic fluid air contamination incident. The temperatures chosen for the evaluation of oil degradation products varied between studies and ranged from 121–371°C (TOX/2006/39 Annexes 10, 11 and 12). The COT noted the theoretical formation of trimethylolpropanephosphate (TMPP) from trimethylolpropane esters and tricresyl phosphates is outlined in annex 10 of TOX/2006/39 but that this could not be demonstrated in experiments using realistic pyrolysis conditions (TOX/2006/39 Annex 11; A72). Thus, it was considered that formation of TMPP during fume contaminant incidents on commercial aircraft was unlikely, although appropriate air monitoring data were not available.

30. Comparatively few data are available on the thermal degradation of hydraulic fluids used in commercial aircraft. Skydrol 500B-4 was heated up to a temperature of 425°C, and after heating, there was no fluid and only a small amount of charred material remained. Tributyl phosphate was identified in the bulk and pyrolysed hydraulic fluid which was reduced to dryness, a low level of carbon monoxide (CO) was produced during pyrolysis, and phenol was present in the pyrolysed fluid.[A6] The thermal and oxidative degradation of triaryl phosphate-based hydraulic fluid at high temperatures leads to the formation of carbon particles, hydrogen and a variety of short chain hydrocarbons which can rearrange to form condensed ring structures.[C73] Some of these reactions can occur at low temperatures but the presence of naphthalene or phenyl acetylene in the fluid implied that most of the reactions took place at temperatures above approximately 750°C. It has been reported that the first step in the thermal degradation of all trialkyl phosphates at 200-300°C is production of phosphoric acid and olefins,[C78] while at 370°C tributyl phosphate would predominantly produce phosphoric acid, butene, 1-butanol, butyraldehyde and butyl ethers.[C79]

31. The COT commented on the high degree of variability documented in the oil pyrolysis studies summarised in annexes 11 and 12 of TOX/2006/39 with respect to the chemical species formed, their concentration in pyrolysed oils, and that there was no apparent reason for the observed variation. Attempts were made to use these data to identify potentially irritant VOCs and semi-volatile organic chemicals (SVOCs), but Members noted the variation between oils regarding the formation of such compounds. It was not possible to predict whether the concentrations and exposures to such compounds would reach a level that could result in irritancy. Hence, the COT considered that, rather than trying to predict what might be present, the best approach would be to obtain real air contamination data under actual flight conditions. The COT considered that appropriate time resolution would be required in any exposure monitoring approach to measure the levels of oil and/or hydraulic fluid pyrolysis products in cabin air during an incident. This would allow actual data on concentrations of chemical contaminants released during an incident to be evaluated. It was concluded that the pyrolysis data presented were informative but could not be used to predict which compounds to measure in

exposure monitoring studies, although additional molecular modelling of pyrolysis might be helpful in this regard (TOX/2006/39 Annex 15).

Exposure monitoring

Information on chemical exposure

Engine test rig

32. One possible approach suggested for determining potential cabin air contaminants resulting from an oil/hydraulic fluid incident might be the use of an engine test rig. Whilst this option has been considered by engine manufacturers, the practical difficulties associated with introducing either a defined level of damage to an oil seal or a known volume of oil could create unrealistic situations and the evaluation of the results would therefore be difficult.

33. A published test rig study attempted to measure bleed air contaminants using a Garrett TPE 331 turboprop engine with an induced oil seal fault (TOX/2006/39 Annex 12). However, the findings would appear to have limited relevance because of the engineering differences between turboprop engines and the turbofan engines used to power commercial jet aircraft. These differences are likely to affect the conditions occurring in the engines during an oil leak e.g. airflow, degree of air compression and temperature.

34. Bleed air tests have been conducted on an ALF502R-5 turbofan engine from a BAe 146 involved in a cabin air incident.[A124,C165] When inspected on the wing of the aircraft, the engine exhibited evidence of a minor oil leak but during the bleed air tests no oil leaks were apparent. The engine was subject to two tests representing the flight profile and bleed air conditions of the incident flight as closely as possible. For each test, the engine was taken from ground idle through take-off, climb, cruise, descent, stabilisation at ground idle and then normal shutdown. Air samples were taken from both the bleed and inlet ducts at ground idle, take-off, climb, cruise and descent test points, and one set of air samples was taken over the entire test interval from initiation of ground idle through to termination of descent. The engine test air samples were analysed for aldehydes, polycyclic aromatic hydrocarbons (PAHs), VOCs, SVOCs, carbon dioxide, carbon monoxide, methane and ozone precursors. Around one hundred compounds were evaluated. Overall, the identities were established of around 90 compounds at the bleed and/or inlet ducts, including alkanes, alkenes and aldehydes. The concentration of the compounds was generally below 12 parts per billion (ppb) at the engine bleed port. Acetone, methylene chloride, carbon monoxide, methane, carbon dioxide, ethylene, 2-methylpentane, 3-methylpentane were detected at varying concentrations above this level in various phases of flight but there were marked differences between the two test runs. Assuming no significant in-cabin sources, the levels of these chemicals would be expected to be lower in cabin air. The ortho- isomer of tricresyl phosphate was not detected but total isomers of tricresyl phosphate had been detected and quantified.

Published and unpublished exposure data from studies of commercial jet aircraft

35. The House of Lords Enquiry in November 2000 concluded that the overriding research need with respect to exposure was to benchmark the air quality in current aircraft, using comprehensive measurements, with agreed methodologies, on a sufficiently large number of flights to be typical, if not fully representative.[C75] A number of observations can be made from the retrieved published studies on exposure measurements.[C56-72]

36. The available studies and reviews cited in the discussion papers reviewed by COT, in which measured exposures to VOCs and SVOCs have been reported, date from the early 1990s and refer to exposure monitoring on commercial aircraft using data from 1-45 non-smoking flights for an individual airframe.[C69] However, the majority of these studies measuring VOC/SVOC levels have examined between only one and approximately 10 flights for any particular aircraft. Thus, most studies provide relatively limited information on potential exposures.

37. No published data regarding air monitoring on the B757 were retrieved. An in-confidence report was obtained for a study undertaken to investigate potential exposure to engine oil, hydraulic fluid, APU oil and fuel using B757s on the ground (to establish methodology) and during 3 commercial flights.[C76] The approach used included photoionisation detection (PID) for real time monitoring for oil vapour and sampling with thermal desorption and analysis for identification and quantification. The B757s selected for this study had been reported previously as having problems with oil smells. The authors report that there was some limited evidence for the presence of APU oil and hydraulic fluid in cabin air on all the flights but at levels below those expected to induce mild acute symptoms. An increase in carbon monoxide was reported on Flight 1 (reported to be well below the World Health Organisation (WHO) air quality guideline) and on the return flight indicating the presence of combustion products. Around 100 individual organic compounds including VOCs and siloxanes were detected using thermal desorption. Concentrations of aldehydes were similar to those that have been found indoors in buildings.[A107] Analysis of reconstructed chromatograms suggested that oil may have been present in some samples coinciding with reports of oily smells. An increase in total VOCs was reported during cruise compared to other phases of flight.

38. Air quality measurements in a number of flights with the B777 and B747 (TOX/2006/39 Annex 12c) indicated VOC levels similar to those reported for indoor air in domestic buildings.[A107] Compounds commonly detected included toluene, limonene, a range of aliphatic hydrocarbons containing 6-7 carbon atoms (including methylcyclohexane) and some volatile oxygenated compounds, the most abundant of which was ethanol.

39. Air quality measurements have been undertaken on a small number of flights in the BAe 146,[C66,C72] and charcoal filters from the aircraft have also been analysed.[C66] Data on analysis of filters and flight deck walls from the

B757 and BAe 146 for tricresyl phosphate isomers was reported to the BALPA conference in April 2005. One HEPA filter from a B757 had 930μg tricresyl phosphate isomers/4.5m^2.[A44] An in-confidence report was submitted detailing a fume incident created deliberately on a BAe 146 by raising the duct temperature to a maximum. For a short time, the duct temperature exceeded 90^{o}C, but normal operating conditions were then reinstated. The acrid smell associated with hot ducts was present during the test. Analyses of air samples taken before and after the event did not identify any SVOCs or VOCs relevant to oil/hydraulic fluid. After the report of a fume event on the same aircraft, the tests were repeated using both the APU and engine with the aircraft both on the ground and in the air. No evidence for the presence of any SVOC or VOC was reported. Nor was any evidence found in subsequent engineering inspections undertaken by the relevant airline.

40. Air quality measurements have been made in a test flight on a BAe 146 aircraft previously involved in a cabin air incident.[C166] The test flight was undertaken with replacement of the faulty engine that was fitted to the aircraft at the time of the incident. Specific flight parameters were recorded including altitude, engine bleed status, fresh/recirculated air ratios and duct temperatures. Cabin air samples taken during the flight were analysed for VOCs, SVOCs, aldehydes and ozone precursors (VOCs that are considered to contribute to the formation of ozone in the right atmospheric conditions), and the aircraft was fitted with portable carbon monoxide and carbon dioxide detectors. Low levels of a wide range of VOCs and SVOCs, aldehydes and ozone precursors were detected. The concentrations of carbon dioxide, carbon monoxide, hydrocarbons, oil degradation products and ozone were below the established CAA, Federal Aviation Administration (FAA) and contractual limits.

41. A number of observations can be made on the existing published data retrieved for the COT. None of the available studies has monitored air quality during an oil/hydraulic fluid smoke/fume incident. The methods of air sampling and analysis vary considerably between studies. A review published in 2000 which presented a consideration of the available published air monitoring studies in commercial aircraft reported that most were deficient in one or more aspects of study design or conduct.[C67] The authors commented on the need for more data using appropriate and reliable methods. The need was also noted for quality assurance of measurements, and for information on detection limits, precision and accuracy with periodic multi-point calibrations. Duplicates and field blanks should be employed.[C67] In one study that attempted to monitor bleed air and cabin air simultaneously, levels of contaminants were often lower in the bleed air than in cabin air indicating in-cabin sources of many VOCs. Where phase of flight was included in a study, levels of VOCs have often been highest on the ground and lower during the phases of flight.[C72] Where there has been some limited evidence for an elevation of exposure to a VOC that might have been related to an oil incident, levels were reported to be below odour thresholds and well below relevant occupational exposure standards. There is also the possibility for some VOCs that there are sources of exposure other than oil contamination incidents. A number of the published studies cited in annex

12c of TOX/2006/39 have investigated SVOCs including tricresyl phosphate isomers, and report no evidence for exposure in aircraft. However, tricresyl phosphate isomers and other SVOCs were extracted from the walls of cabin air supply ducts removed from BAe 146 aircraft documented in a CAA report.[A67] In-confidence information provided to the COT documented evidence for the presence of tricresyl phosphate isomers and absence of TMPP on air filters and wall swabs taken from a number of B757 aircraft. The identity of the tricresyl phosphate isomers and their concentrations was unstated (TOX/2006/21 Annex 8).

42. Overall, the dearth of available information from exposure monitoring means that no definite conclusions can be reached on the normal range of air contaminants and their concentrations in commercial aircraft during flight.

43. The available data from exposure studies presented to the COT point to the complexity of the variables that would need to be considered in any future monitoring exercise regarding the normal background range of air contaminants and also, during an oil/hydraulic fluid contamination incident. These variables include the type of oil and hydraulic fluid used, engine type and maintenance, the design and operation of the air conditioning system and the flight parameters. Overall, the COT agreed that there was considerable uncertainty regarding the identity and levels of VOCs, SVOCs and other pyrolysis products released into the cabin air during oil or hydraulic fluid smoke/fume incidents. It was agreed that the concept of a test rig for identifying compounds that might be released into bleed air systems was potentially desirable but impractical, due to the uncertainty of the relevance of the data that would be obtained, and therefore the investigation should be undertaken on appropriate aircraft during flight (TOX/2007/10 Annex 1). Any exposure monitoring approach that was developed would need to link to data recorded by airlines with regard to the engineering status of the aeroplane and reports of odours and adverse symptoms by pilots and other crew. Further consideration of exposure monitoring is presented in paragraphs 64-72 and in the research discussion section in paragraphs 73-83 of this statement.

<u>Information on incident reporting</u>

Pilot reporting

44. Flight crew communicate all issues that might require engineering intervention (e.g. blown light bulbs and system failures, which are not necessarily safety incidents) to engineers using a Tech Log, or its equivalent depending on the airline. Pilots do not have to make a mandatory entry in the Tech Log regarding cabin air events and hence this system may not record all events.

45. The Air Safety Report (ASR) is a formal means of communication between the flight crew and the airline regarding any safety incident deemed worthy of reporting. The pilot can indicate that the event reported in the ASR reaches the threshold for a CAA MOR. Pilots do not necessarily have to

make an ASR in relation to cabin fume events. In addition, airlines screen the ASRs they receive with regard to whether a MOR should be raised and will submit any ASR a pilot considers reaches the threshold for a MOR to the CAA. The CAA classification of MORs can be conceived as a pyramid ranging from a very small number of accidents that require major and immediate intervention through incidents, undesirable events and abnormal variations to normal variations which constitute the majority of MORs received. Cabin fume events are most likely not to reach the threshold for a MOR or, if they do, they are most likely to represent a small part of the abnormal variations/normal variations. Individual airlines would consider the threshold for submitting MORs on a case-by-case basis. Most cabin fume events would, if reported, be documented as ASRs or possibly as Tech Logs but would not necessarily generate an automated Flight Data Monitoring (FDM) record.

46. BALPA presented information that there was underreporting of the wide range of smells encountered on board aircraft, some of which might be transient oil incidents, but it was not possible to make any estimate of how many were due to oil/hydraulic fluid contaminants as opposed to food and toilet smells. The COT considered that it was unclear to what extent oil/hydraulic fluid smoke/fume events go unrecorded as no clear distinction was made between the detection of, for example, toilet/galley and oil fumes.

BALPA database analysis

47. The BALPA database relates to 770 reports between 1 May 1985 - 4 April 2006 (after removal of duplicates and reports for which no data were identified). Only limited information was entered on the BALPA database: incident date, airframe type, CAA MOR reference number and a brief note of the incident. The analysis was restricted to the BAe146/BAe AvroRJ and B757 aircraft as these airframe types had most reports of smoke/fume incidents entered on the BALPA database. An increase in the incidence of reporting is evident from around 1999/2000 onwards. The data analysis included airframe types, flight phases, odour descriptions, health symptoms and results of engineering investigations. The limited extent of reporting on the BALPA database may underestimate the incidence of adverse symptoms and a more systematic approach with objective standards set for the reporting of incidents would help to resolve the uncertainties and inconsistencies in the data. A comparison was made between the BALPA smoke/fume incident and CAA MORs for the period 1 January 2001 – 4 April 2006. An attempt to estimate the total number of smoke/fume incidents in British regulated airlines was made by the COT Secretariat using a ‘capture-recapture method’ that has been applied to estimate the size of human populations.

48. The COT evaluated the BALPA database and data submitted from the CAA MOR database. It was noted that BALPA did not use a standardised questionnaire and thus the details provided varied considerably. It was noted that the CAA MOR database was aimed primarily at identifying aircraft malfunctions and included a series of technical questions, some of which requested information on adverse health symptoms. The COT consider that

perception of smoke/fumes could have influenced a pilot's reaction to an incident and whether or not they completed an ASR. It was agreed that the reporting of smoke/fume incidents was to some extent subjective and would depend on whether individual pilots felt there was a need to report an incident.

49. It was noted that both databases were likely to be incomplete and that there were limitations in a capture-recapture analysis in estimating the total number of incidents worldwide. The Deputy Chair noted that the pilots who had written to him had all considered that underreporting of possibly minor fume incidents was widespread. It was agreed that a detailed evaluation of the extent of underreporting in the existing databases was not possible, but that objective monitoring of exposure and health would be a priority for the future.

Pilot health

Review and evaluation of epidemiological data

50. The COT agreed that even the best quality epidemiological studies evaluated in this review had not measured exposure or had investigated only a small number of cabin air contaminants. Members noted that an evaluation of incidents from the BALPA and CAA databases, including those with reported health information, had been undertaken. The Committee considered specifically a number of epidemiological studies identified as being relevant to the consideration of health symptoms reported by pilots and identified as such during the BALPA conference held in April 2005.

51. The available epidemiological studies (cross-sectional, case studies, case series) had been systematically reviewed by the DH Toxicology Unit. The Committee were satisfied with the quality of the review and agreed the evaluation of the studies undertaken. On the basis of the review, the Committee concluded that it was not possible to determine whether a causal association exists between cabin air exposures (general or following incidents) and ill-health (acute or chronic) among flight crew. The inability to reach such a conclusion was based on the lack of studies specifically designed to address this question systematically. Members considered that while there is a large body of anecdotal and descriptive evidence on possible associations of health symptoms with cabin air quality (paragraph 53), such data do not meet the standard of a properly designed and performed epidemiological study necessary to reach definite conclusions.

52. The COT concurred with the overall conclusions reached in the review, subject to the limitations of the underlying studies and their health/exposure assessment methods, and agreed that the further additional literature searching proposed was unlikely to alter the conclusions reached:

a. Some aircrew who report incidents experience a variety of health symptoms including some suggestive of irritant (eye/nose/throat/skin) symptoms.

b. Some, but not all aircrew perceive an association between their symptoms and i) cabin air quality (CAQ) in general and/or ii) CAQ incidents.
c. Aircrew report more concerns about CAQ than office workers do about air quality in buildings.
d. Symptoms have been reported more frequently among certain occupational groups than others as follows: aircrew > teachers or office workers; female aircrew > male; younger crew > older (with some exceptions).
e. Among aircrew, symptom reporting varies by employment status and occupation, with higher rates reported among current Italian flight attendants than former Italian flight attendants (based on one study), and among cabin crew than cockpit crew.
f. Symptom reporting has been higher for certain flight characteristics: longhaul > shorthaul; return flights > outbound; night flights > daytime; no humidification > humidification; no catalytic converters > converters
g. Symptom reporting may be higher for certain aircraft types: for example, B767 > DC9 (no air recirculation); jet > propeller; B747SP (flies at higher altitude) > B747.

53. A review of case reports, incidents and testimonies (TOX/2007/20 Annex 5) provided to the COT supplemented the overview of epidemiological studies (TOX/2007/10 Annex 10) and information from the BALPA database and CAA MOR evaluation reported to the COT (TOX/2006/21 Annexes 3 and 4). The following related conclusions are reached, subject to the limitations of the underlying case reports, incident reports, and testimony transcripts/submissions:

a. Aircrew experienced a variety of health symptoms in association with reported individual or repeated cabin air incidents.
b. Most reported health symptoms were acute in nature.
c. Although less frequent, some aircrew report longer-term symptoms.
d. The cabin air incidents have been collectively and generally described as odours, fumes or smoke.

54. Testimonies submitted by individuals to the COT Secretariat were considered and evaluated for their inclusion in the epidemiology overview. Overall, the Committee considered that there were a number of oil/hydraulic fluid contamination incidents with reports of plausible acute adverse symptoms, but the frequency of such incidents could not be determined.

<u>Evaluation of BALPA database for acute and chronic health symptoms</u>

55. An overview was undertaken of the reports in the BALPA database regarding health symptoms. Acute symptoms predominantly relating to the eyes, nose, throat, mouth, chest and the presence of nausea occurred with similar frequency in the BAe 146 and the B757 (the highest prevalence of acute symptom was approximately 8% of the evaluated reports for both aircraft types). Acute neurological symptoms of headache, dizziness, and light-headedness occurred again with roughly similar prevalence for both

aircraft types. (The highest prevalence for an acute neurological effect of headache was approximately 14% of the evaluated reports for BAe 146/Avro RJ and 10% for the B757.) Chronic neurological symptoms such as tingling of limbs, tingling of the tongue, memory loss and impaired concentration were found less frequently (the highest prevalence for chronic neurological symptoms was $\leq$ 3%.) An evaluation of non-specific symptoms (e.g. ‘unwell’, tiredness, ‘effects’, ‘incapacitation’) and indicated that these too were less frequent (the highest prevalence was approximately 5% of evaluated reports).

56. Members noted that the types of symptoms reported in the BALPA database were common in healthy individuals as is illustrated by findings for recipients of placebos in phase one clinical trials, in studies of indoor air quality, and in surveys of the general population.[C170-C175] The evaluation of adverse health symptoms would benefit from information on comparable control populations e.g. aircrew on planes where fume incidents had not been identified, but care would be needed to take account of possible recall bias.

57. Some further consideration of possible approaches to the investigation of sensory irritation that may be experienced by pilots in commercial aircraft is given in the discussion and research section paragraphs 73-83 of this statement.

Neuropsychological investigations of pilots

58. The COT received a report of a neuropsychological evaluation of eighteen self-selected pilots, nine of whom were still flying. The Committee received independent expert advice on neuropsychology and agreed that caution was required in assessing the results of this evaluation. The COT agreed that although the pattern of neuropsychological impairment reported was not consistent amongst the pilots, overall the potential for cognitive deficits needed further consideration. Members noted that this was a small-scale evaluation and consider that it would be necessary to conduct a further study with appropriate controls before any firm conclusions can be drawn. Members noted a peer-reviewed published reference to variation in the outcome of the Weschler Adult Intelligence Scale – Third Edition (WAIS-III) test dependent on the level of experience of the individual conducting the test.

Consideration of the neuropsychological symptoms reported in pilots and OP exposure.

59. The COT considered the evidence presented in the BALPA conference proceedings and in the additional papers submitted by BALPA. Members agreed that, on the basis of the available evidence, it was important to keep an open mind regarding the possible identity of potential risk factors and health effects in pilots. It was the view of Members that there had been an emphasis on the potential involvement of OPs in health symptoms reported by commercial airline pilots in the BALPA submission. The COT consider that there might be a number of candidate chemicals, one of which are OPs, and the Committee felt that focusing on OPs drew attention away from other potential chemical causes. The COT in 1999 concluded that 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. Members noted that similar patterns of symptoms have been reported in studies of other syndromes such as 'sick-building syndrome' not involving OP exposure. Members consider that, irrespective and independent of chemical exposure, the combination of odour perception, discomfort, involuntary exposure and stressful working conditions in a commercial aircraft cabin environment could lead to long-term health effects through non-toxic mechanisms in a small proportion of individuals.

Consideration of the neuropsychological symptoms reported in pilots and carbon monoxide exposure

60. The COT noted that neuropsychological symptoms attributed to carbon monoxide were either transient during moderate exposures, or seen as lasting after-effects of exposures that resulted in severe carbon monoxide poisoning and agreed that carbon monoxide was unlikely to be the cause of the reported neuropsychological impairment in pilots. However, Members noted that there was some uncertainty in that the exposures to carbon monoxide during an oil/hydraulic fluid smoke/fume incident had not been measured and also with regard to the possibility of prolonged low level exposure in commercial aircraft which needed to be examined in the proposed research. These gaps in knowledge would be addressed in the research that is proposed. Members considered that the reduced oxygen pressures in commercial aircraft at high altitude (cabin pressurisation is to 8000 feet) would have a marginal affect on the risk assessment for exposure to carbon monoxide. The COT received an independent expert opinion suggesting that lower oxygen pressure at 8000 feet would not modify the potential effects of carbon monoxide or alter the air quality standards necessary for protection of health.

Pilot skill tests and proficiency checks and their value to neuropsychological evaluation of pilots

61. The COT concurred with an independent neuropsychologist that pilot skill tests and proficiency checks were task orientated evaluations and would detect only gross neuropsychological deficits in pilots. Such deficits had been described in some individuals. Members consider that follow-up of pilots who failed skill and proficiency tests might be a useful approach to identify retrospectively pilots for further epidemiological study. This aspect is considered in more detail in the research discussion section paragraphs 73-83 of this statement.

<u>Evaluation of pilot blood/fat tissue bioanalyses and clinical chemistry data</u>

62. The results of blood/fat tissue bioanalyses were submitted in a report to the COT. Twenty self-selected pilots gave blood and/or fat samples for the analysis of levels of VOCs and pesticides. Some of the pilots self-selected between blood and fat samples on the basis of whether they suspected recent exposure or were concerned about past, chronic exposure but specific time-lapse criteria were not applied to the results. The blood and fat samples were

analysed by headspace gas chromatography with flame ionisation detection (GC-FID) to quantify VOC concentrations, cell-free DNA and DNA adduct formation with organic chemicals and metals.

63. The COT considered the bioanalytical methods used in the report submitted, including the presentation of results and their interpretation. Significant doubt was placed on the interpretation of reportedly increased levels of solvents in pilots due to a lack of data on method precision, and limitations identified in the origin and application of the population 'average' figures. Consequently, no analyte concentration could be derived for any of these individuals with confidence. Nor could any cause-and-effect relationship be established. The possible use of biomonitoring data is considered further in the discussion and research section paragraphs 73-83 of this statement.

COT discussion and consideration of further research

Exposure monitoring

64. The DfT specifically asked the Committee to advise on any further research required to evaluate this area as part of the referral.

65. One of the initial stages involves the determination of the identity and concentration of chemical compounds and any particulates that might be present in cabin air under normal conditions and during an oil/hydraulic fluid smoke/fume incident. The approaches and devices used in the initial stages of the strategy must fulfil certain functional requirements in terms of the range and concentration of VOCs and SVOCs monitored and compliance with air-worthiness standards (e.g. potential electromagnetic interference). It was noted that the initial methods/prototype devices must not distract pilots and crew from their duties, either during normal conditions of flight or during an incident and that, as far as possible, prototype devices should be automated or require minimal human input to set-up and operate, and be easy to access and maintain. It was noted that there are severe space restrictions in the cockpit, and that in both the cockpit and cabin environment the air inlets and outlets tend to be covered by grilles. It was noted that there is a need to reach agreement with airlines on monitoring strategies and that the size of equipment used in many of the monitoring studies might be one obstacle to obtaining airline agreement for undertaking studies involving a large number of flights.[C68]

66. The COT agreed there was considerable uncertainty regarding the identity of any VOCs, SVOCs and other pyrolysis products released into the cabin air during an oil or hydraulic fluid smoke/fume incident (paragraph 43 above and TOX/2007/10 Annex 1). Members considered that approaches to exposure measurement should cover the widest possible range of potential contaminants from oil/hydraulic fluid that could be analysed and should not focus on only a single chemical group. Also, the investigation should be undertaken on appropriate aircraft (e.g. B757s fitted with the RR535C engine

identified by the COT as one possible aircraft to use) during flight (TOX/2007/10, Annex 1).

67. The COT agreed that the starting point for developing an approach to exposure monitoring should be the data from pilot reports and on the rate of engineering-confirmed oil incidents which would be informative for identifying the type of aircraft and number of flights to be included in studies. Members discussed whether it was possible to formulate a specific health related hypothesis in the exposure monitoring studies at this stage (e.g. exposure to a range of specified pyrolysis chemicals is associated with acute ill-health such as irritancy and this might be a marker for exposures associated with chronic ill-health) or whether the initial phase of exposure monitoring should be to enable hypotheses to be generated. Overall, it was felt that no specific hypothesis regarding which chemicals to monitor could be pursued at the present time and thus a staged approach to exposure monitoring and data collection from pilots (e.g. health assessment) would be most appropriate, to enable specific hypotheses to be developed and investigated.

68. The COT was provided with estimates of the number of flights that would need to be monitored for air quality in order to have a 95 percent probability of monitoring at least one flight in which an oil/hydraulic fluid smoke/fume incident occurred, assuming the underlying rate of such incidents was 1/100, 1/1000 or 1/10,000 flights. The COT agreed that there would need to be monitoring on approximately 300, 3000 or 30,000 flights respectively (per airframe with a specific engine).

69. Members agreed that the calculated incidence of oil/hydraulic fluid fume contamination was approximately 1% from pilot reports and approximately 0.05% following engineering investigation (although this might vary depending on airframe, engine type and servicing). It was noted that the estimates of incident rates and numbers of sectors required to be monitored were preliminary and should be used for initial guidance only. It was evident from this information that overall a large number of sectors would need to be monitored to have a high degree of confidence of including an engineering-confirmed oil/hydraulic fluid smoke/fume incident. Members agreed the proposed preliminary estimates of the number of flights required for exposure monitoring per airframe/engine type of more than 100 sectors for background monitoring, and of up to 10,000-15,000 sectors to assess exposures relating to engineering-confirmed oil/hydraulic fluid smoke/fume incidents, depending on the airframe and engine type, APU, rate of oil/hydraulic fluid contamination, air conditioning system operation and engine servicing. Members noted that such a study would also provide more reliable data on background exposure.

70. Members considered a wide range of analytical techniques, samplers and sensors that could be used or adapted to undertake the initial assessment of the cockpit/cabin environment (TOX/2006/39, Annex 15) in conjunction with data presented on oil content and combustion analyses, potential smoke/fume incident rates, the number of aircraft types and the number of flights/sectors that may need to be sampled. It was agreed that time weighted solid phase microextraction (SPME) would be most practical

given the large number of compounds to be detected/analysed, the cost of such devices and acceptability to commercial airlines. Members recognised that SPME would not allow monitoring of peak air concentrations during an oil/hydraulic fluid contamination incident as it produces time integrated average concentrations. Nevertheless, it would be an important step in obtaining background information on cabin air environment and could lead to more targeted studies in the future. The COT agreed that SPME devices would need validation, including calibration with chemicals that might be involved in cabin air smoke/fume incidents. The choice of chemicals for calibration should take into account the range of volatility of chemicals that might be present in the cabin environment. The analytical methods used would have to be precise, accurate, robust and fully validated. Members considered that short duration flights should be monitored to maximise the chance of monitoring an oil/hydraulic fluid contamination incident.

71. Members agreed that a two-stage approach to exposure monitoring is needed, with an initial validation of SPME technology followed by preliminary air monitoring testing using appropriate B757 and BAe 146 aircraft (defined in paragraph 67 above). These preliminary air monitoring investigations would need to collect data on pilot reports of oil/hydraulic fluid smoke/fumes from ASR forms and data on flight operations (such as Quick Access records). It would also have to take into account the often transient nature of contamination incidents. It was anticipated that the initial air monitoring studies would provide some information regarding the cabin environment in the B757 and BAe 146 linking to flight operations but it would not be possible or feasible to obtain full information to assess potential health effects from ASR forms. Such further studies would require enhanced cabin air monitoring and further consideration of health data to be collected from pilots. Members noted that molecular modelling of pyrolysis might be of use as an aid for compound identification in the initial air monitoring studies.

72. Members noted that carbon monoxide could be used as one potential indicator of burning oil and asked that monitoring of carbon monoxide be included in any exposure monitoring approach. It was noted that the DfT propose using PIDs for carbon monoxide and VOC detection in the research to be funded.

Epidemiology

73. The COT have been asked to review the BALPA submission and based on the data submitted by BALPA and that sourced by the COT Secretariat, to assess the risk of exposure of aircrew (particularly pilots) to OPs and oil/hydraulic fluid pyrolysis products in cabin air and to determine whether there is a case for a relationship between exposure and the ill-health in aircraft crews (c.f. paragraph 15i of this statement).

74. Members note the conclusion reached from the DH Toxicology Unit overview of epidemiology that it was not possible to conclude whether a causal association exists between cabin air exposures (either general or following incidents) and ill-health in commercial aircraft crews (paragraph 51).

However, there were a number of oil/hydraulic fluid contamination incidents where the temporal relationship between reports of exposure and acute health effects provided evidence that an association was plausible. The Committee agreed that consideration should be given to further research investigating a possible association between exposure to oil/hydraulic fluid pyrolysis products and ill-health in aircrews. In this respect our main focus, as specified in the referral to the COT, has been to consider further research with respect to commercial airline pilots. Thus, in relation to the provision of advice to the DfT as requested in paragraph 15ii of this statement, three research questions can be identified:

i. Are substances released into commercial aircraft via the bleed system that could potentially be harmful to health?

ii. Are exposures to such substances likely to result in acute ill-health symptoms?

iii. Are exposures to such substances likely to result in chronic health symptoms?

75. It was noted that the cabin environment on commercial aircraft represents a very specific occupational setting and that the proposed strategy for research on exposure and potential ill-health in pilots should take a staged approach to the evaluation of exposure and potential adverse health effects with consideration of the results of investigations at each stage to inform on future research questions. The COT considered that any epidemiological study would need some index of oil/hydraulic fluid air contamination incident exposure in order to be useful.

76. In relation to question 74i), regarding the potential release of harmful substances into bleed air on commercial aircraft, Members consider that the approach to exposure monitoring developed in paragraphs 64-72 of this statement represents the most appropriate and pragmatic way forward. It was noted that aircrew involved in the exposure monitoring phase of research will be asked to fill in ASRs to record reports of odours and/or symptoms. Whilst this will not systematically record all the information that could be obtained through administration of a specific questionnaire on air quality and health effects, it was considered a pragmatic approach using reporting procedures that would be regarded as normal by aircrew, and for which compliance is likely to be relatively high.

77. Members considered the general aspects of the use of biological monitoring data from pilots with alleged exposure to oil/hydraulic fluid contaminants. It was agreed that such monitoring might be performed after the proposed air sampling and in response to specific health-related questions/hypotheses. COT members considered that unless biological samples (e.g. urine, blood) were taken and analysed within an appropriate short time period, usually within12-24 hours after an oil/hydraulic fluid contamination incident, then the results of the analyses were unlikely to be informative with regard to actual exposure or in linking exposure with reported

acute health effects. Members agreed that the usefulness of performing chemical analysis on tissue samples (e.g. blood, urine, adipose tissue, hair, nails) obtained from pilots would depend on the toxicokinetics of the chemicals of interest. It is possible that biological monitoring for carboxyhaemoglobin levels in pilots could be undertaken as part of a future epidemiological study, but only if the results of the air monitoring studies described in paragraphs 64-72 of this statement suggest this would be valuable.

78. In relation to question 74ii), the COT was aware that symptoms of sensory irritancy (e.g. eye and respiratory tract irritancy) were amongst the most common complaints reported in pilots (paragraph 55).[C170-C175] Members have considered a general structure-activity equation which could be used to predict whether exposure to mixtures of VOCs and SVOCs were above or below a threshold for sensory irritancy.[C111] The COT agreed that in principle the approach could be used to evaluate measured levels of air pollution in aircraft, provided it had been properly validated. Validation could involve blind predictions of sensory irritancy thresholds for chemicals with published sensory threshold data, and predictions of sensory irritancy thresholds for chemicals followed by laboratory testing with subsequent threshold testing. The interpretation of any results derived from application of predictive algorithms for sensory irritancy would also need to take into account the large number of potentially confounding factors (such as low humidity) that might be associated with sensory irritant responses in pilots. This research would provide a crude indication/semi-quantitative measure of whether exposures in cabin air might be associated with sensory irritation.

79. The COT concluded that there was no scope for the use of animal models to explore further potential acute and chronic health effects reported to be associated with oil/hydraulic fluid contamination events in commercial aircraft, until the potential chemical exposures are better characterised.

80. With regard to the design of epidemiological studies to investigate acute and chronic health effects in pilots (questions 74ii and 74iii), Members confirm the need for objective as well as subjective measures of exposure in such studies. This could come from exposure monitoring or by use of a validated proxy measures, such as work on different types of aircraft. It was agreed that there is insufficient evidence to justify epidemiological research focusing specifically on exposure to OPs.

81. Members have considered the report of the neuropsychological evaluation in self-selected pilots and sought independent expert advice (paragraph 58). The COT agreed there was limited evidence regarding neuropsychological impairment in pilots. Overall, the Committee concluded that the available evidence, although limited, together with information from pilots supported further investigation of neuropsychological impairment in commercial pilots. However, the Committee also agreed that there was insufficient evidence to recommend any specific additional research for any other acute or chronic health effect with regard to oil/hydraulic fluid contamination incidents on commercial aircraft.

82. There are essentially two approaches that could be used to further investigate evidence for neuropsychological impairment in commercial pilots. The first would focus on pilots who failed the routine proficiency testing. This would have the advantage of increasing the power of the study to detect possible causes of ill-health. A disadvantage would be the possibility that pilots who failed the proficiency tests were not representative of UK commercial pilots in any association between exposure and neuropsychological deficit. The alternative approach would be a cross-sectional survey of current and past pilots, focussing initially on the findings from neuropsychological tests in relation to relatively simple, proxy measures of exposure (e.g. comparisons between pilots who flew different airframe/engine combinations and between pilots who had reported previous oil/hydraulic fluid contamination incidents and those who had not reported such events). The potential for confounding by tendency to somatise would have to be taken into consideration in such a study. There would be considerable merit in international collaboration in such research given the likely number of pilots required for such a study. To avoid missing a problem through selective exclusion of pilots who had retired because of impaired health, it would be advisable to include former pilots who had left the profession, for example within the past 5 years.

83. The proposed cross-sectional study, which would be relatively costly, would answer the following questions: to what extent do the prevalence of neuropsychological symptoms and the results of neuropsychological testing differ between pilots who have flown different airframes/engine combinations, and between pilots who report or do not report air contamination incidents, and do these associations differ by country. The study would not address whether neuropsychological symptoms occur at a different prevalence to that in the general population.

COT conclusions

84. The Committee agreed the following overall conclusions with regard to the questions posed which are reproduced below for ease of reference:

i. Evaluate the BALPA submission and, based on the data submitted by BALPA and that sourced by the Secretariat, assess the risk of exposure of aircraft crews to OPs and oil/hydraulic fluid pyrolysis products in cabin air and determine whether there is a case for a relationship between exposure and the ill-health in aircraft crews.

ii. Provide the DfT with appropriate advice on any further research required to evaluate this subject.

85. The COT considered as a general point, prior to detailed evaluation of the submitted evidence that regardless of the cause(s) of the reported adverse symptoms, it would be prudent to take appropriate action to prevent oil or hydraulic fluid smoke/fume contamination incidents (paragraph 28).

86. 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 (paragraphs 54 and 74).

Exposure

87. There was considerable uncertainty regarding the identity of VOCs, SVOCs and other pyrolysis products released into the cabin air during an oil/hydraulic fluid smoke/fume incidents (paragraph 43). Approaches to exposure measurement should address the widest possible range of potential contaminants from oil/hydraulic fluid that could be analysed and should not focus on only a single chemical group or compound (paragraph 66).

88. No specific hypothesis regarding which chemicals to monitor could be pursued at the present time and thus a staged approach to exposure monitoring and data collection from pilots (e.g. health assessment) would be most appropriate, to enable specific hypotheses to be developed and investigated (paragraph 67).

89. Available options for exposure monitoring and passive sampling of a large number of flights on appropriate aircraft represent the best initial approach (paragraphs 69 and 70). A two-stage approach to exposure monitoring needed to be undertaken, with validation and calibration of SPME technology followed by preliminary air monitoring testing using appropriate B757 and BAe 146 aircraft (paragraph 71). The preliminary air monitoring investigations would need to collect data on pilot reports of oil/hydraulic fluid smoke/fumes and data on flight operations. Molecular modelling of pyrolysis could be used as an aid for compound identification in the initial studies (paragraphs 31 and 71).

90. Any exposure monitoring approach that is developed would need to link to data recorded by airlines with regard to engineering status of the aircraft and reports of odours and adverse symptoms by pilots. It would also have to take into account the often transient nature of contamination incidents (paragraph 71).

91. Carbon monoxide could be used as one potential indicator of burning oil and thus the measurement strategy should include monitoring for carbon monoxide exposure (paragraph 72).

Health

92. In order to address concerns about incident-related acute irritation, a general structure-activity equation might, in principle, be used to evaluate the acute sensory irritancy thresholds of mixtures present in cabin air incidents

after independent validation of the approach to sensory irritants (paragraph 78). The outcome of this research would provide an indication/semi-quantitative measure as to whether exposures in commercial aircraft cabin air might be associated with sensory irritation. Overall, there was insufficient evidence available to the COT to recommend additional epidemiological research on any acute health effects (paragraph 81).

93. We confirm the need to obtain objective measures of exposure in epidemiological studies (paragraph 75). These could come from exposure monitoring or through use of validated proxy measures of exposure. There was insufficient evidence to justify epidemiological research focusing specifically on OPs (paragraphs 80 and 82).

94. The available evidence, although limited, together with information from pilots supported further investigation of neuropsychological impairment in commercial pilots (paragraphs 58 and 81). However, there was insufficient evidence to recommend any specific additional research for any other acute or chronic health effect with regard to oil/hydraulic fluid contamination incidents on commercial aircraft (paragraph 81).

95. The most appropriate epidemiological approach to research on neuropsychological status in commercial pilots would be a cross-sectional study to investigate how the prevalence of reported neuropsychological symptoms and the results of neuropsychological testing differ between pilots flying different airframes/engine combinations and between pilots who report, or do not report, air quality incidents, and whether associations differ between countries. Such a study would need the development and use of a validated proxy exposure approach for oil/hydraulic fluid contamination exposure in order to determine whether there is an association between oil/hydraulic fluid smoke/fume contamination and neuropsychological effects (paragraph 83).

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<u>References</u>

Submission A references

A1. Cox, L., Michaelis, S. (2002). A survey of health symptoms in BAe 146 aircrew. J. Occup. Health Safety – Aust NZ, 18(4), 305-312.

A2. Michaelis, S. (2003). A survey of health symptoms in BALPA Boeing 757 pilots. J. Occup. Health Safety, Aust. NZ, 19, 253-261.

A3. Rayman, R.B., McNaughton, G.B. (1983). Smoke/fumes in the cockpit. Aerospace Medical Association August 1983, pp. 738-740. *Page 739 not supplied.*

A4. Winder, C., Fonteyn, P., Balouet, J.-C. (2002). Aerotoxic syndrome: a descriptive epidemiological survey of aircrew exposed to in-cabin airborne contaminants. J. Occup. Health Safety – Aust. NZ, 18, 321-338.

A5. van Netten, C. (1998). Air quality and health effects associated with the operation of BAe 146-200 aircraft. Appl. Occup. Environ. Hyg, 13, 733-739. *Pages 734, 736 and 738 not supplied*

A6. van Netten C. (2000). Analysis of two jet engine lubricating oils and a hydraulic fluid: Their pyrolytic breakdown products and their implications on aircraft air quality. From: Air Quality & Comfort in Airliner Cabins, ASTM –STP 1393, N.L. Nagda, Ed., American Society for Testing and Materials, West Conshohocken, P.A. pp.61-75.

A7. Fox, RB. (2000). Air Quality and Comfort Measurement Aboard a Commuter Aircraft and Solutions to Improve Perceived Occupant Comfort Levels. From: Air Quality and Comfort in airliner Cabins, ASTM STP 1393, N. L. Nagda, Ed., American Society for Testing and Materials, West Conshohocken, PA, 2000.

A8. Capt Dave Hopkinson (1998). Air Safety Report.

A9. Michaelis, S., Winder, C. (2005). Aircraft Air Quality Malfunction Incidents: Causation, regulatory, reporting and rates. Environmental chemistry, Springer Verlag only) (accepted for publication, draft copy).

A10. Michaelis, S., Best, R. (2005). Aircraft Air Quality Malfunction Incidents: Design, Servicing, and Policy Measures to Decrease Frequency and Severity of Toxic Events. Environmental chemistry, Springer Verlag (accepted for publication, draft copy).

A11. Association of Flight Attendants, AFL-CIO, Washington, DC (2003). Aircraft Air Quality: What's wrong with it and what needs to be done. Submitted to The Aviation Subcommittee of The Transportation and Infrastructure Committee U.S. House of Representatives, June 4th 2003.

A12. Cox, L. (Australian Federation of Air Pilots; AUS-ALPA) and Michaelis, S. (2001). Aircraft Air Supply Contamination, November 2001.

A13. Winder, C., Balouet, J.-.C. (2001). Aircrew exposure to chemicals in aircraft: symptoms of irritation and toxicity. J. Occup. Health Safety - Aust NZ, 17, 471-483.

A14. DeHart, R.L. (1999). Airline passengers with multiple chemical sensitivity. (Abstract).

A15. Allied Signal Aerospace (1997). Air Quality Aboard Ansett Airlines BAe 146 Aircraft: Final Report, November 25th 1997. *Pages missing.*

A16. Allied Signal Aerospace (1991). Results of air quality testing for Dan Air, London: Memorandum from Richard Fox, July 22nd 1991.

A17. van Netten, C. (2002). Analysis and implications of aircraft disinsectants. The Science of the Total Environment, 293, 257-262.

A18. Ansett Australia Update No 8: Flight Attendant Department (1998).

A19. Ansett Australia, External Panel of Specialists (1998). Consensus Statement: BAe 146 Odour Occurrences, Brisbane, 25th March 1998.

A20. Media Release (2002). Ansett Claim Settled, July 2002.

A21. Michaelis, S. (2003). Appendix 3 (Masters Thesis?): Sample Reporting from various sources. UNSW, December 2003.

A22. Michaelis, S. (2003). Appendix 4 (Masters Thesis?): Number of Cabin Contamination reports. UNSW, December 2003.

A23. van Netten, C. (2000). Analysis of two jet engine lubricating oils and a hydraulic fluid: Their pyrolytic breakdown products and their implications on aircraft air quality. From: Air Quality & Comfort in Airliner Cabins, ASTM –STP 1393, N.L. Nagda, Ed., American Society for Testing and Materials, West Conshohocken, P.A. pp.61-75. *Not provided.*

A24. ATSB (2001). Recommendations R20010092 & R20010093 –12th April 2001.
The citations actually supplied were ATSB R19990052 (06/09/99) and R19990053 (06/09/99). (R20010092 & R20010093 were obtained from ATSB website, www.atsb.gov.au).

A25. ATSB (2003). British Aerospace plc BAe 146 Fume Incident. Australian Transport Safety Bureau, Occurrence: 200205307, 11th January 2002.

A26. ATSB (2003). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200205865, 2nd December 2002.

A27. ATSB (2002). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200103238, 18th July 2001. *Document not supplied.*

A28. ATSB (2003). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200204912, 20th October 2002.

A29. ATSB (2003). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200203030, 29th June 2002. *Document not supplied.* (Document obtained from ATSB website (www.atsb.gov.au).

A30. ATSB (2000). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200002431, 30th April 2000.

A31. ATSB (2002). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200103696, 7th August 2001.

A32. ATSB. British Aerospace plc BAe 146 - Australian Transport Safety Bureau, Occurrence: 200102467. *Document not supplied.* (Document obtained from ATSB website (www.atsb.gov.au).

A33. ATSB (1999). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 199702276, 10th July 1997.

A34. ATSB (2001). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200000176, 21st January 2000.

A35. ATSB (2000). British Aerospace plc BAe 146 Incident. Australian Transport Safety Bureau, Occurrence: 200001331, 13th April 2000 / 200001175, 31 March, 2000.

A36. Australian Industrial Relations Commission (2003). Pavlinovich, Nevan Phillip v National Jet Systems Pty Ltd, May 2003.

A37. Australian Senate Inquiry (2000). BAe 146 cabin Air Quality: Submission by Dr. J. Burdon & Andrew Thom; Volume 1.

A38. Balouet, J.C., Hoffman, H. and Winder, C. (1999). Aviation and exposure to toxic chemicals. American Institute of Aeronautics and Astronautics, Washington D.C., document 1999-01-5603, ISSN 0148-7191.

A39. Winder, C. and Weber, R. (eds) (2001). Aviation air quality: proceedings of the aviation air quality symposium, Australian Defence Force Academy, UNSW, Canberra, 7 December 2000. Reports in Safety and Environmental Science, August 2001.

A40. British Aerospace Systems (2001). BAe 146 Manufacturer's Operations Manual: Notice to Aircrew, Operational Notice: No. OP 16 (Issue 1). Smoke and Fumes. January 2001.

A41. British Aerospace Systems (2001). All Operator Message Ref. 00/030V: Smoke and Fumes (Smells), January 2001.

A42. Balouet, J.C. (1998). In-cabin trace chemicals and crew health issues. Aerospace Medical Association annual meeting, Seattle, 20th May 1998.

A43. Balouet, J.-C., Kerguelen, M., Winder, C. (2001). Toxicity and hypoxia: hyperbaric pressure and LC50s for carbon monoxide or hydrogen cyanide. International Congress of Toxicology, Brisbane, 8th-12th July 2001. Toxicology, 164, Abstract P3D15, p 164.

A44. BALPA 'Contaminated Air Protection Conference' - London – 20th-21st April 2005. – BUNDLE.

A45. Bureau of Air Safety Investigation (1997). Preliminary Report 9702276, British Aerospace plc BAe 146-300, 10th July 1997.

A46. Haley, R.W., Marshall, W.W., McDonald, G.G. (2000). Brain Abnormalities in the Gulf War Syndrome: evaluation with MR spectroscopy. Radiology, 215, 807-817.

A47. British Aerospace (1991). Complaint or Difficulty Report, Report No 27803, 10th February 1991.

A48. BAe 146 - List of Service Bulletins re fumes etc..

A49. British Aerospace (1984). Service Information Leaflet 21/7: Oil contamination of air conditioning system, December 1984..

A50. Air Accidents Investigation Branch (2004). BAe 146-200, G-JEAK. Aircraft accident report no: 1/2004 (EW/C2000/11/4).

A51. BAE SYSTEMS (Operations) Limited (2001). Bae 146 series/AVRO 146-RJ series aircraft inspection service bulletin, ISB 21-150, 20th March 2001. Air conditioning – to inspect engine oil seals, APU and ECS jet pump and air conditioning pack for signs of oil contamination.

A52. BAE SYSTEMS (Operations) Limited (2002). BAe 146 series/AVRO 146-RJ series aircraft– inspection service bulletin – ISB. 21-156, 31st October 2002. Air conditioning – to inspect engine oil seals, APU and ECS jet pump and air conditioning pack for signs of oil contamination.

A53. BAE SYSTEMS (2001). All Operator Message: Ref 01/004V, 14th February 2001. Revision of BAe 146 & Avro RJ MOM Vol.3 – Abnormal and Emergency Checklist - Smoke & Fumes.

A54. BAE SYSTEMS (Operations) Limited (2003). Modification Service Bulletin BAe 146 series/Avro 146 RJ series aircraft, SB.49-036-36019E Revision 4, 30th April 2003. Airborne auxiliary power (APU): Introduction of improved APU inlet flexible duct part no. DXA07175.

A55. BAE SYSTEMS (2000/2001). BAe 146/RJ service information leaflet Ref: 21-45, Nov 2000/Jan 2001. Cabin air quality troubleshooting advice and relevant modifications.

A56. BAE SYSTEMS (1990/1991). BAe 146/RJ service information leaflet.– Ref: 21/27, 28th September 1990/ 20th February 1991. Oil contamination of air conditioning system.

A57. British Aerospace (1991). Letter to Mr J Nicholson, Engineering Manager, East West Airlines (Operations) Ltd, 10th July 1991.

A58. Civil Aviation Authority, Flight Operations Department (2001). Communication 14/2001, 24th August 2001.

A59. Civil Aviation Authority, Safety Regulation Group – Safety Investigation and Data Department (2004). Follow-up action on occurrence report: incident involving BAe 146-200, G-Jeak, descent to Birmingham airport on 5 November 2000 (fumes in cockpit). CAA factor number F12/2004, 20th February 2004.

A60. Civil Aviation Authority, Safety Regulation Group (2001). PubRel – B757 smoke/fumes on flight deck, 13th June 1996 to 13th June 2001. *Pages missing (2, 4, 6, 8, 10, 12, 14 and 17).*

A61. Civil Aviation Authority, Safety Regulation Group – Safety Investigation & Data Department (2003). PubRel – B757 smoke and fumes, 1st September 2001 to 21st January 2003.

A62. Civil Aviation Authority, Safety Regulation Group, Safety Investigation & Data Department (2004). PubRel – BAe 146 – smoke/fumes on the flight deck, 1st Jan 1980 – 15th March 2004.

A63. Civil Aviation Authority, Safety Regulation Group (2003). Safety Initiative - Hazardous contamination of flight deck cabin air.

A64. Civil Aviation Authority, Safety Regulation Group, Medical Division (2000). Letter from Dr S Janvrin to Dr M G P Fisher, 11th December 2000.

A65. Civil Aviation Authority, Safety Regulation Group, Medical Division (2000). Letter from Dr S. Janvrin to Mr. J.F. Soddy, 11th December 2000.

A66. Civil Aviation Authority, Safety Regulation Group (2002). Flight Operations Department Communication (FODCOM) 21/2002. 1- UK public transport smoke/fumes occurrences. 2- Emergency procedures for cabin altitude warning.

A67. Civil Aviation Authority, Safety Regulation Group (2004). CAA paper 2004/04: cabin air quality.

A68. Wright, J., Clarke, D. (International Cabin Crew Health Foundation) (1999). Cabin crew syndrome: a case study - acute and chronic symptoms. A presentation to the ASHRAE aviation subcommittee, 26th January 1999.

A69. Newman, David (2001). –CASA, CO Pilot, Flight Safety Australia, November-December 2001.

A70. Newman, David (1999). CASA, Fit To Fly? Flight Safety Australia, November-December 1999.

A71. Hoy, Bob (CASA - What Makes an Aircraft Airworthy - FSA, May-June 2000 - Bob Hoy. *Document not supplied – printed from CASA website.*

A72. van Netten, C., Leung, V. (2000). Comparison of the constituents of two jet engine lubricating oils and their volatile pyrolytic degradation products. Appl. Occup. Environ. Hyg., 15, 277-283.

A73. Harper, A.C. (2001). Corporate affiliation bias and BAe 146 aircraft: Senate report. Australia and New Zealand Journal of Public Health, 25 (page number not clear).

A74. Winder, C., Michaelis, S. (2005). Crew effects from toxic exposures on aircraft. (Draft copy - accepted for publication in Environmental Chemistry, Springer Verlag).

A75. Kelso, A.G., Charlesworth, J.M., McVea, G.G. (1988). Contamination of environmental control systems in Hercules aircraft. Department of Defence, Defence Science and Technology Organisation, Materials Research Laboratory, Melbourne, Victoria: Report MRL-R-1116, April 1988.

A76. Wagner, Sheldon L. Diagnosis and treatment of organophosphate and carbamate intoxication. *Article source and date not detaile*d.

A77. Michaelis, S.. (2002). Aircraft cabin fumes: an aviation safety issue. J. Occup. Health Safety – Aust. NZ, 18, 291-294.

A78. Examples of rates of Fume Events From various Sources. *Article source and date not clear*.

A79. Balouet, J.-C., Winder, C. Exposure to Contaminants at Altitude and the Associated Toxicity Increases. *Full reference details not provided*.

A80. Airworthiness standards: transport category airplanes. Federal Aviation Regulation Part 25 Sec. 25.831, 2nd January 1965.

A81. Villiers, D., Pattie, D. (2004). Airworthiness: Watching brief. Flight Safety Australia, January-February 2004.

A82. Montgomery, M.R., Wier, G.T., Zieve, F.J., Anders, M.W. (1977). Human intoxication following inhalation exposure to synthetic jet lubricating oil. Clin. Toxicol., 11, 423-426.

A83. Van Netten, C., Leung, V. (2001). Hydraulic fluids and jet engine oil: pyrolysis and aircraft air quality. Arch. Environ. Health, 56, 181-186.

A84. Pezzoli, G., Canesi, M., Antonini, A. et al. (2000). Hydrocarbon exposure and Parkinson's disease. Neurology, 55, 667-673.

A85. Hocking, M.B. (1998). Indoor air quality: recommendations relevant to aircraft passenger cabins. American Industrial Hygiene Association Journal, 59, 446-454.

A86. Singh, B. (Senior Research Officer, Aviation Medicine, Royal Australian Air Force) (2004). In-Flight Smoke And Fumes. *Source not specified*.

A87. Encyclopaedia of Occupational Health and Safety 4th ed. (1997?). Stellman, J.M. ed., International Labour Office, Geneva. *Selected pages on Sick Building Syndrome and Multiple Chemical Sensitivity*.

A88. International Programme on Chemical Safety (1998).Concise international chemical assessment document N°9. *N*-phenyl-1-naphthylamine. World Health Organisation, Geneva.

A89. International Programme on Chemical Safety (1990). Environmental Health Criteria 110. Tricresyl Phosphate. World Health Organisation, Geneva.

A90. Bobb, A.J. (2003). Known Harmful Effects of Constituents of Jet Oil Smoke. Naval Health Research Centre Detachment (Toxicology), Wright-Patterson AFB, OH, February 2003.

A91. Welshons, W.V., Thayer, K.A., Judy, B.M. et al. (2003). Large effects from small exposures. I. Mechanisms for endocrine-disrupting chemicals with estrogenic activity. Environmental Health Perspectives, 111, 994-1006.

A92. Traylor, D. (1986). Oil fumes in the air conditioning system. Lockheed Service News, 13(2), April-June 1986.

A93. Jamal, G.A. (1995). Long term neurotoxic effects of organophosphate compounds. Adverse Drug React. Toxicol. Rev., 14, 85-99.

A94. Winder, C. (2002). Mechanisms of multiple chemical sensitivity. Toxicology Letters, 128, 85-97.

A95. Health and Safety Executive (1998). Medical aspects of work-related exposures to Organo-phosphates. Guidance Note MS 17, draft revision 23rd November 1998.

A96. Health and Safety Executive (2000). Medical aspects of work-related exposures to organophosphates. Guidance Note MS 17, third edition 2000.

A97. Winder, C. (1998). Misuse of the exposure standard concept. –J. Occup. Health Safety – Aust. NZ, 14, 107-110.

A98. Mackerer, C.R., Ladov, E.N. (Mobil Business Resources Inc.) (2000). On the inquiry into: air safety – BAe 146 cabin air quality. Submission to the Senate References Committee - Rural & Regional Affairs and Transport.

A99. Mackerer, C.R. (2000). Mobil Business Resources Corporation letter to Dr Jean Christophe Balouet, 28th February, 2000.

A100. Esso Petroleum Company, Limited (2004). Mobil Jet Oil II safety data sheet - UK version, revision date 24th May 2004.

A101. Mobil Corporation (1996). Mobil Jet Oil II – material safety data bulletin - US version.

A102. Mobil Oil Corporation and Affiliated Companies (1998). Mobil Jet Oil II Oil Can Label.

A103. Mobil Oil Review of papers - Limited review only.

A104. Ladov, E.N. (1983). Mobil Jet Oil II. Mobil Oil Corporation, Environmental Affairs and Toxicology Department New York, correspondence to J. Aveni, 24th January 1883.

A105. van Netten, C. (1999). Multi-elemental analysis of jet engine lubricating oils and hydraulic fluids and their implication in aircraft air quality incidents. The Science of the Total Environment,;229, 125-129.

A106 . National Academy of Sciences (1986). The airliner cabin environment: air quality and safety. National Academy Press, Washington D.C.

A107. National Academy of Sciences (2002). The airliner cabin environment and the health of passengers and crew. National Academy Press, Washington D.C.

A108. Wizniak, E.P. (1983). Special investigation - an evaluation of the potential for turbine oil by-product contamination of an aircraft's cabin environmental system. National Transportation Safety Board Bureau of Technology, Group Chairman's report of special investigation, 25th April 1983.

A109. Jamal, G.A. (1997). Neurological syndromes of organophosphorus compounds. Adverse Drug React. Toxicol. Rev., 16,133-170.

A110. Murata, T., Kimura, H., Kado, M. et al. (2001). Neuronal damage in the interval form of CO poisoning determined by serial diffusion weighted magnetic resonance imaging plus H-magnetic resonance spectroscopy. Journal of Neurology, Neurosurgery and Psychiatry, 71, 250-253.

A111. Coxon, L. (2002). Neuropsychological assessment of BAe 146 aircraft crew members exposed to jet engine oil emissions. Journal of Occupational Health and Safety, Australia and New Zealand, 18, 313-319.

A112. Heuser, G., Mena, I. (1998). Neurospect in neurotoxic chemical exposure demonstration of long-term functional abnormalities. Toxicology and Industrial Health, 14, 813-827.

A113 . NTP - Chemical Repository (1991). Tri-O-Cresyl Phosphate - CAS NO 78-30-8, Radian Corporation, 29th August 1991.

A114. NTP - Chemical Respitory (1991) - Tri-O-Cresyl Phosphate - CAS NO 1330-78-5. Radian Corporation, 29th August 1991.

A115. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (1999). Organophosphates: executive summary.

A116. Abou-Donia, M.B. (2003). Organophosphorus ester-induced chronic neurotoxicity. Arch. Environ. Health, 58, 484-497.

A117. Winder, C. Problems of the separation of health and safety in the aviation industry: a case study of the BAe 146. *Full reference details not provided*.

A118. Report to ATSB (1998).

A119. SAE Aerospace (2004). Airborne chemicals in aircraft cabins. Aerospace information report - AIR4766/2, August 2005.

A120. Walker, P.H. (Rolls-Royce plc) (1990). Discussion on the specification limit for total organic material in cabin bleed air. SAE - E31 cabin air sub-committee discussion paper, October 1990, Williamsburg VA.

A121 . SAE (1981). Environmental control system contamination. Aerospace information report AIR 1539, 30th January 1981, Warrendale PA.

A122 . Gorey, N., Morrisson, G. (RAAF) (1999). School of Mathematics and Statistics, University College, ADFA.

A123. Senate Rural and Regional Affairs and Transport Relations Committee (2005). Report on Air Safety and Cabin Air Quality in the BAe 146 Aircraft. 5 VOLUMES OF EVIDENCE & FINAL REPORT. Parliament of Australia, Canberra, October 2000.

A124. Statens Haverikommission (SHK) board of accident investigation (Sweden) (1999). Report RL 2001:41e. Incident onboard aircraft SE-DRE during flight between Stockholm and Malmo, M county, Sweden, on 12 November 1999. Case L-102/99.

A125. Summary of studies citing association with MS/MND & OPs. *Full reference details not provided.*

A126. The Airliner Cabin Environment Report Response Team (ACERRT) (2002). Report to the Administrator on the National Research Council Report, “The Airliner Cabin Environment and the Health of Passengers and Crew”, 6th February, 2002.

A127. Cripe, L.I. (1996). The MMPI in neuropsychological assessment: a murky measure. Applied Neuropsychology, 3/4, 97-103.

A128. Winder, C., Balouet, J.-C. (2002). The toxicity of commercial jet oils. Environmental Research Section A, 89,146-164.

A129. Winder, C., Balouet, J.-C. (2000). Aerotoxic syndrome: adverse health effects following exposure to jet oil mist during commercial flights. *In:* Towards a safe and civil society. Proceedings of the international congress of occupational health conference, Brisbane, Australia, 4-6 September 2000, Eddington, I. ed., ICOH, Brisbane (Eddington, I., ed.), pp.196-199.

A130. Glanville, A.R., Burdon, J. (2004). Toxic planes: the respiratory effects of flying. Sydney Thoracic Society Meeting, 2004.

A131. Transport Safety Bureau of Canada (2000). Interim air safety recommendations - Swissair Flight 111 Accident, 4th December, 2000.

A132. UK DoH (1999). Toxicology of OPs and the mechanisms involved. Chapter 5 (pp 49-58) in: Organophosphates. *Committee on Toxicity of Chemicals in Food, Consumer Products and the Environmen*t. UK Department of Health, HMSO, London, 1999. (COT REPORT).

A133. Weber, R.O., Winder, C. (2000). The December 2000 aviation air quality symposium: consensus statement. University Of New South Wales,– 7th December 2000.

A134. Cripe, L.I. (1999?). Use of the MMPI with mild closed head injury. *Date and source not indicated on document.*

A135. Kesler, S.R., Hopkins, R.O., weaver, L.K. et al. (2001). Verbal memory deficits associated with fornix atrophy in carbon monoxide poisoning. Journal of the International Neuropsychological Society, 7, 640-646.

A136. Abou-Donia M.B. (2003). Organophosphorus Ester-Induced Chronic Neurotoxicity. Arch. Env. Health, 58, 484-497.

A137. Akgura, S.A., O¨ ztu¨rka, P. Solakb, I. et al. (2003). Human serum paraoxonase (PON1) activity in acute organophosphorous insecticide poisoning. Forensic Science International, 133, 136-140.

A138. Axelrada J.C., Howard, C.V., McLean, W.G. (2002). Interactions between pesticides and components of pesticide formulations in an in vitro neurotoxicity test. Toxicology, 173, 259-268.

A139. Blain, P.G. (2001). Adverse health effects after low level exposure to organophosphates. Occup. Environ. Med., 58, 689-690, 2001.

A140. de Blaquie`re, G.E., Waters, L., Blain, P.G., Williams, F.M. (2000). Electrophysiological and biochemical effects of single and multiple doses of the organophosphate diazinon in the mouse. Toxicol. Appl. Pharmacol., 166, 81-91.

A141. Buchanan, D., Pilkington, A., Sewell, C. et al. (2001). Estimation of cumulative exposure to organophosphate sheep dips in a study of chronic neurological health effects among United Kingdom sheep dippers. Occup. Environ. Med., 58, 694-701.

A142. Burnley, I.H. (1995). Socioeconomic and spatial differentials in mortality and means of committing suicide in New South Wales, Australia, 1985-91. Soc. Sci. Med., 41, 687-698.

A143. Carruth, A.K., Logan, C.A. (2002). Depressive symptoms in farm women: effects of health status and farming lifestyle characteristics, behaviours and beliefs. Journal of Community Health, 27, 213-228.

A144. Cherry, N., Mackness, M., Durrington, P. et al. (2002). Paraoxonase (PON1) polymorphisms in farmers attributing ill-health to sheep dip. Lancet, 359, 763-764.

A145. Cocker, J.,Mason, H.J., Garfitt, S.J., Jones, K. (2002). Biological monitoring of exposure to organophosphate pesticides. Toxicology Letters, 134, 97-103.

A145a . Winder, C. (2005). Proceedings of the BALPA Air Safety and Cabin Air Quality International Aero Industry Conference. Held at Imperial College, London, 20-21 April, 2005. *Data source supplied but not cited on summary list.*

A145a . International aero industry conference: contaminated air protection – air safety and cabin air quality. Proceedings of the BALPA air safety and cabin air quality international aero industry conference, held at Imperial College, London, 20-21 April 2005. Reports in Safety and Environmental Science, August 2005 (draft).

A146. Coggon, D. (2002). Work with pesticides and organophosphate sheep dips – an in-depth review. Occup. Med, 52, 467-470, 2002

A147. Colosio C., Tiramani, M., Maroni, M. (2003). Neurobehavioral effects of pesticides: state of the art. NeuroToxicology, 24, 577-591.

A148. Costa, L.G., Richter, R.J., Li, W.-F. et al. (2003). Paraoxonase (PON1) as a biomarker of susceptibility for organophosphate toxicity. Biomarkers, 81, 1-12, 2003.

A149. Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (1999) Organophosphates. UK Department of Health.

A150. Dam, K., Seidler, F.J., Slotkin, T.A. (2003). Transcriptional biomarkers distinguish between vulnerable periods for developmental neurotoxicity of chlorpyrifos: implications for toxicogenomics. Brain Research Bulletin, 59, 261-265.

A151. Davies, R., Ahmed, G., Freer, T. (2000). Chronic exposure to organophosphates: background and clinical picture. Advances in Psychiatric Treatment, 6, 187-192.

A152. Duggan, A., Charnley, G., Chen, W. et al. (2003). Di-alkyl phosphate biomonitoring data: assessing cumulative exposure to organophosphate pesticides. Regulatory Toxicology and Pharmacology, 37, 382-395.

A153. Farahat, T.M., Abdelrasoul, G.M., Amr, M.M. et al. (2003). Neurobehavioural effects among workers occupationally exposed to organophosphorous pesticides. Occup. Environ. Med., 60, 279-286.

A154. Finkelstein, B.L., Benner, E.A., Hendrixson, M.C. (2002). Tricyclic cyanoguanidines: synthesis, site of action and insecticidal activity of a novel class of reversible acetylcholinesterase inhibitors. Bioorganic & Medicinal Chemistry, 10, 599-613.

A155. Handy, R.D., Abd-El Samei, H.A., Bayomy, M.F.F. et al. (2002). Chronic diazinon exposure: pathologies of spleen, thymus, blood cells, and lymph nodes are modulated by dietary protein or lipid in the mouse . Toxicology, 172, 13-34.

A156. Hovey, J.D., Magan, C. (2000). Acculturative stress, anxiety, and depression among Mexican immigrant farmworkers in the midwest United States. Journal of Immigrant Health, 2, 119-131.

A157. Jamal, G.A., Hansen, S., Julu, P.O.O. (2002). Low level exposures to organophosphorous esters may cause neurotoxicity. Toxicology, 181-182, 23-33.

A158. Jamal, G.A., Hansen, S., Pilkington, A. et al. (2002). A clinical neurological, neurophysiological, and neuropsychological study of sheep farmers and dippers exposed to organophosphate pesticides. Occup. Environ. Med., 59, 434-441.

A159. Johnson, J.L., Cusack, B., Hughes, T.F. et al. (2003). Inhibitors tethered near the acetylcholinesterase active site serve as molecular rulers of the peripheral and acylation sites. J. Biol. Chem., 278, 38948-38955.

A160. Karalliedde, L.D., Edwards, P., Marrs, T.C. (2003). Variables influencing the toxic response to organophosphates in humans. Food Chem. Tox., 41, 1-13.

A161. Khurana, D., Prabhaker, S. (2000). Organophosphorus intoxication. Neurology, 57, 600-602.

A162. Koskinen, O., Pukkila, K., Hakko, H. et al. (2002). Is occupation relevant in suicide? Journal of Affective Disorders, 70, 197-203.

A163. Lee, B.W., London, L., Paulauskis, J. et al. (2003). Association between human paraoxonase gene polymorphism and chronic symptoms in pesticide-exposed workers. J. Occup. Environ. Med, 45, 118-122.

A164. Lockwood, A.H. (2004). Human testing of pesticides: ethical and scientific considerations. Amercian Journal of Public Health, 94, 1908-1916.

A165. Lockwood, A.H. (2002). Organophosphate pesticides and public policy. Current Opinion in Neurology, 15, 725-729.

A166. London, L., Flisher, A.J., Wesseling, C. et al. (2005). Suicide and exposure to organophosphate insecticides: cause or effect? American Journal of Industrial Medicine, 47, 308-321.

A167. Mackness, B., Durrington, P., Povey, A. et al. (2003). Paraoxonase and susceptibility to organophosphorous poisoning in farmers dipping sheep. Pharmacogenetics, 13, 81-88.

A168. Malmberg, A., Hawton, K., Simkin, S. (1997). A study of suicide in farmers in England and Wales. Journal of Psychosomatic Research, 43, 107-111.

A169. Manninen, P., Heliovaara, M., Riihimaki, H., Makela, P. (1997). Does psychological distress predict disability? International Journal of Epidemiology, 26, 1063-1070.

A170. Moretto, A., Lotti, M. (1998). Poisoning by organophosphorus insecticides and sensory neuropathy. J. Neurol. Neurosurg. Psychiatry, 64, 463-468.

A171. Nishimura, M., Terao, T., Soeda, S. et al. (2004). Suicide and occupation: further supportive evidence for their relevance. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 28, 83-87.

A172. Ohayo-Mitoko G.J.A., Kromhout, H., Simwa, J.M. et al. (2000). Self reported symptoms and inhibition of acetylcholinesterase activity among Kenyan agricultural workers. Occup. Environ. Med., 57, 195-200.

A173. O'Malley, M. (1997). Clinical evaluation of pesticide exposure and poisonings. Lancet, 349, 1161-1166.

A174. Parron, T., Hernandez, A.F., Villanuevah, E. (1996). Increased risk of suicide with exposure to pesticides in an intensive agricultural area. A 12-year retrospective study. Forensic Science International, 79, 53-63.

A175. Pilkington, A., Buchanan, D., Jamal, G.A. et al. (2001). An epidemiological study of the relations between exposure to organophosphate pesticides and indices of chronic peripheral neuropathy and neuropsychological abnormalities in sheep farmers and dippers. Occup. Environ. Med., 58, 702-710.

A176. Prendergast, M., Terry, A.V., Buccafusco, J.J. (1998). Effects of chronic, low-level organophosphate exposure on delayed recall, discrimination, and spatial learning in monkeys and rats. Neurotoxicology and Teratology, 20, 115-122.

A177. Ray, D.E. (1998). Chronic effects of low level exposure to anticholinesterases - a mechanistic review. Toxicology Letters, 102-103, 527-533.

A178. Ray, D.E., Richards, P.G. (2001). The potential for toxic effects of chronic, low-dose exposure to organophosphates. Toxicology Letters, 120, 343-351.

A179. Salvi, R.M., Lara, D.R., Ghisolfi, E.S. et al. (2003). Neuropsychiatric evaluation in subjects chronically exposed to organophosphate pesticides. Toxicological Sciences, 72, 267-271.

A180. Scarth, R.D., Stallones, L., Zwerling, C., Burmeister, L.F. (2000). The prevalence of depressive symptoms and risk factors among Iowa and Colorado farmers. American Journal of Industrial Medicine, 37, 382-389.

A181. Simkin, S., Hawton, K., Fagg, J., Malmberg, A. (1998). Stress in farmers: a survey of farmers in England and Wales. Occup. Environ. Med., 55, 729-734.

A182. Singh, S., Sharma, N. (2000). Neurological syndromes following organophosphate poisoning. Neurol. India, 48, 308-313.

A183. Sogorb, M.A., Vilanova, E. (2002). Enzymes involved in the detoxification of organophosphorus, carbamate and pyrethroid insecticides through hydrolysis. Toxicology Letters, 128, 215-228.

A184. Stallones, L., Beseler, C. (2002). Pesticide poisoning and depressive symptoms among farm residents. Ann. Epidemiol., 12, 389-394.

A185. Stallones, L., Beseler, C. (2002). Pesticide illness, farm practices, and neurological symptoms among farm residents in Colorado. Environmental Research Section A, 90, 89-97.

A186. Steenland, K. (1996). Chronic neurological effects of organophosphate pesticides. BMJ, 312, 1312-1313.

A187. Stephens, R., Spurgeon, A., Calvert, I.A. et al. (1995). Neuropsychological effects of long-term exposure to organophosphates in sheep dip. Lancet, 345, 1135-1139.

A188. Stephens, R., Spurgeon, A., Berry, H. (1996). Organophosphates: the relationship between chronic and acute exposure effects. Neurotoxicology and Teratology, 18, 449-453.

A189. Swisher, R.R., Elder, G.H., Lorenz, F.O., Conger, R.D. (1998). The long arm of the farm: how an occupation structures exposure and vulnerability to stressors across role domains. Journal of Health and Social Behavior, 39, 72-89.

A190. Teke, E., Sungurtekin, H., Sahiner, T. et al. (2004). Organophosphate poisoning case with atypical clinical survey and magnetic resonance imaging findings. J. Neurol. Neurosurg. Psychiatry, 75, 936-939.

A191. Vidair, C.A. (2004). Age dependence of organophosphate and carbamate neurotoxicity in the postnatal rat: extrapolation to the human. Toxicology and Applied Pharmacology, 196, 287-302.

A192. Watterson, A.E. (1999). Regulating pesticides in the UK: a case study of risk management problems relating to the organophosphate diazinon. Toxicology Letters, 107, 241-248.

A193. Worth, J. (2002). Paraoxonase polymorphisms and organophosphates. Lancet, 260, 802-803.

Submission B references

B1. Air quality in airplane cabins and similar environments. Edited by Hocking, M.B. Volume 4 Air Pollution, Part H The Handbook of Environmental Chemistry. Published Springer, Berlin Heidelberg, 2005.

B2. Protect your office in the sky- report all contaminated air events. BALPA, undated.

B3. HSE EH40/2005 workplace exposure limits.

B4. Odor thresholds for chemicals with established occupational health standards. US AIHA1989 (reprint 1997), pp 1-11.

B5. BSR ASHRAE proposed new standard 161, Air quality within commercial aircraft. American Society of Heating, Refrigerating and Air-conditioning Engineers, Inc, First public review, September 2005.

B6. ASHRAE proposed new guideline 28, Air quality within commercial aircraft. American Society of Heating, Refrigerating and Air-conditioning Engineers, Inc, First public review, September 2005.

B7. International Aero Industry Conference. Contaminated Air Protection: air safety and cabin air quality. Proceedings of the BALPA air safety and cabin air quality international aero industry conference. Held at Imperial College, London, 20-21 April 2005. Winder, C. (ed.).

B8. Fume database. BALPA.

B9. Research Summary.

B10. BAe 146 Bulletin.

B11. Report to the Administrator on the National Research Council Report "The Airliner Cabin Environment and the Health of Passengers and Crew". Prepared by The Airliner Cabin Environment Report Response Team, 6th February 2002.

B12. Aerospace information report – Airborne Chemicals in Aircraft Cabins. SAE Aerospace, (2004).

B13. US Air Force Armstrong laboratory: Inhalation toxicity of vapour phase lubricants. Lipscomb, J. et al., October 1995.

B14. Mineral oil. ACGIH NIICS/CS/2004/Mineral Oil_2003-08-04, 2004.

B15. Australian parliament hansard dated 21/09/03.

B16. Australian Department of Defense. DSTO Materials Research Laboratory, Melbourne Victoria report MRL-R-116, April 1988.

B17. Commonwealth of Australia – Rural and Regional Affairs and Transport References Committee, 17th August 2000.

B18. Commonwealth of Australia – Rural and Regional Affairs and Transport References Committee, 1st May 2000.

B19. Parliament of Australia – The Senator John Woodley "Air Safety and Cabin Air Quality in the BAE 146 Aircraft".

B20. Commonwealth of Australia – rural and regional affairs and transport references committee, 1st November 1999.

B21. Commonwealth of Australia – rural and regional affairs and transport references committee, 10th April 2000.

B22. Commonwealth of Australia – rural and regional affairs and transport references committee, 14th March 2000.

B23. Commonwealth of Australia – rural and regional affairs and transport references committee, 13th March 2000.

B23a. [citation supplied but not listed] Commonwealth of Australia – rural and regional affairs and transport references committee, 2nd February 2000.

B24. Commonwealth of Australia – rural and regional affairs and transport references committee, 1st February 2000. Transcript of Australian Senate Committee hearing "Air safety – BAe 146 cabin air quality".

B25. Commonwealth of Australia – rural and regional affairs and transport references committee, 2nd November 1999.

B26. Winder, C., Michaelis, S. (2005). Crew effects from toxic exposures on aircraft. Hdb Env. Chem., 4 Part H, 223-242.

B27. Murawski, J. (2005). Occupational and public health risks. The Handbook of Environmental Chemistry Volume 4, Published online, Springer Berlin/Heidelberg, 8th August 2005.

B28. Aircraft air quality malfunction incidents: causation, regulatory, reporting and rates. Winder, C., Michaelis, S. (2005) . The Handbook of Environmental Chemistry Volume 4, Published online, Springer Berlin/Heidelberg.

B29. Aircraft air quality malfunction incidents: Design, servicing, and policy measures to decrease frequency and severity of toxic events. Best, R., Michaelis, S. (2005).The Handbook of Environmental Chemistry Volume 4, Published online, Springer Berlin/Heidelberg.

B30. House of Lords Questions

B31. House of Commons Q and A 2003/4.

B32. House of Commons Q and A 1999-2001.

B33. Label of Mobil Jet Oil II.

B34. Exposure standards for atmospheric contaminants in the occupational environment. Guidance Note [NOHSC:3008(1995)]; National Exposure Standards [NOHSC:1003(1995)], Australia, May 1995.

B35. Control of Substances hazardous to Health Regulations 1999. Approved code of practice for general COSHH, carcinogens and biological agents. Health and Safety Commission.

B36. AAIB reports (citing numbers not yet obtained from AAIB, 6/11/05).

B37. Department of Transport – AAIB.

B38. Air Accident Investigation Ireland.

B39. Appendix E – AAIB Bulletin No 7/2005.

B40. Brown, M.A. (1998). Review of health consequences from high-, intermediate- and low-level exposure to organophosphorus nerve agents. J. Appl. Toxicol., 18, 393-408.

B41. Jamal, G.A. et al. (2002). Low level exposure to organophosphorous esters may cause neurotoxicity. Toxicology, 181-182, 23-33.

B42. Michaels, D. (2005). Manufacturing uncertainty: Contested science and the protection of the public's health and environment. American Journal of Public Health, 95, No. S1, S39-48.

B43. Michaels, D. (2005). Doubt is their product. Scientific American, June 2005, 96-101.

B44. Abou-Donia, M.B., Garrettson, L.K. (2000). Detection of neurofilament autoantibodies in human serum following chemically induced neurologic disorder: a case report. Environmental Epidemiology and Toxicology, 2, 37-41.

B45. El-Fawal, H.A.N. et al. (1999). Neuroimmunotoxicology: humoral assessment of neurotoxicity and autoimmune mechanisms. Environmental Health Perspectives Supplements, 107, S5, 767-775.

B46. Material safety data sheet: mixed octylated diphenylamine and N,N-diphenyl-p-phenylamine. R.T. Vanderbilt Company, Inc.

B47. Materials Safety Data Sheet; Skydrol LD-4 (A00000043). Solutia Australia, 13th November 1998.

B48. Tricresyl phosphate isomers found by R Fox, Allied Signal; minutes of meeting 11, 7th November 1997.

B49. Carbon monoxide.

B50. Letter from J.C. Plummer (manager, Aviation Lubricant Sales, Mobil Oil Australia Limited) to the Sentate Rural and Regional Affairs and Transport References Committee, Australia, 7th October 1999.

B51. B-naphthylamine, CAS: 91-59-8.

B52. 1-Naphthylamine,N-phenyl-, CAS: 90-30-2.

B53. 2-Naphthylamine,N-phenyl-, CAS: 135-88-6.

B54. Tri-o-cresyl phosphate, CAS: 78-30-8. NTP chemical repository, Radian Corporation, 29th August 1991.

B55. N-phenyl-1-naphthylamine. WHO International Programme on Chemical Safety, CICAD N°9.

B56. Letter from P.D. Clark (Manager Medical/EHS, Mobil Oil Australia Ltd), 25th August 1997 to Mr. B. Lodge (Group Manager – Aircraft Safety Regulation, National Jet Systems Group).

B57. FAX from Martin Webb (EH&S Manager, Mobil Oil Australia Ltd) to Dr Dai Lewis (Medical Director, Ansett Australia), 23rd May 1997.

B58. BP turbo oil 25, 2197, 2380, 2389. Safety data sheet, Air BP International, 1st January 2001.

B59. Daughtrey, W. et al. (1996). Subchronic delayed neurotoxicity evaluation of jet engine lubricants containing phosphorous additives. Fundamental and Applied Toxicology, 32, 244-249.

B60. Montgomery, M.R. et al. (1977). Human intoxication following inhalation exposure to synthetic jet lubricating oil. Clin. Toxicol., 11, 423-426.

B61. Letter from Mobil Business Resources corporation to Chris Winder, February 28th 2000.

B62. Mackerer, C.R. et al. (1999). Comparison of neurotoxic effects and potential risks from oral administration or ingestion of tricresyl phosphate and jet engine oil containing tricresyl phosphate. J. Toxicol. Environ. Health, part A, 56, 293-328.

B63. Freudenthal, R.I. et al. (1993). Subchronic neurotoxicity of oil formulations containing either tricresyl phosphate or tri-orthocresyl phosphate. J. Am. College Toxicol., 12, 409-416.

B64. Craig, P.H., Barth, M.L. (1999). Evaluation of the hazards on industrial exposure to tricresyl phosphate: a review and interpretation of the literature. Submitted to Journal of Toxicology and Environmental Health, Part B.

B65. An assessment of the risks of delayed neurotoxicity from industrial and commercial uses of tricresyl phosphate. Mobil, 3rd July 1990.

B66. Allied Signal/Mobil Oil coordination meeting. Allied Signal Aerospace, 3rd January 1996.

B67. Mobil Technical Aviation Symposium October 25, 1996: Allied Signal 85 Series Auxiliary Power Units. AlliedSignal Aerospace, 25th October 1996

B68. 2-Naphthylamine Substance profile.

B69. Material safety data bulletin: 430207-00 Mobil Jet Oil II. Printed for AOPIS, 22nd September 2003.

B70. Material safety data bulletin: Jet Oil II. Mobil Oil Australia Limited, August 1998.

B71. Re: Labelling of Mobil Jet Oil II and 254. Letter from E.N. Ladov (Manager, Product Stewardship & Toxicology, Mobil Business Resources Corporation) to Mr. Julian C. Plummer (Mobil Oil Australia Ltd.), 30th April 1998.

B72. Material safety data sheet: Mobil Jet Oil 2. Mobil Oil Australia Limited, 4th June 1996.

B73. Health effects of oil mists; a brief review. Mackerer, C.R. (1989). Toxicol. Ind. Health, 5, 429-440.

Further identified references

C1. Lindgren, T., Norback, D. (2005). Health and perception of cabin air quality among Swedish commercial airline crew. Indoor Air, 15 Suppl. 10, 65-72.

C2. Rafnsson, V., Olafsdottir, E., Hrafnkelsson, J. et al. (2005). Cosmic radiation increases the risk of nuclear cataract in airline pilots: a population-based case-control study. Arch. Ophthalmol., 123, 1102-1105.

C3. Pombal, R., Peixoto, H., Lima, M., Jorge, A. (2005). Permanent medical disqualification in airline cabin crew: causes in 136 cases, 1993-2002. Aviat. Space Environ. Med., 76, 981-984.

C4. DeHart, R.L. (2003). Health issues of air travel. Annu. Rev. Public Health, 24, 133-151.

C5. Nagda, N.L., Koontz, M.D. (2003). Review of studies on flight attendant health and comfort in airliner cabins. Aviation, Space, and Environmental Medicine, 74, 101-109.

C6. Cavallo, D., Tomao, P., Marinacciso, A. et al. (2002). Evaluation of DNA damage in flight personnel by Comet assay. Mutation Research, 516, 148-152.

C7. Lim, M.K. (2002). Cosmic rays: are air crew at risk? Occup. Environ. Med., 59, 428-432.

C8. Brown, T.P., Shuker, L.K., Rushton, L. et al. (2001). The possible effects on health, comfort and safety of aircraft cabin environments. J. R. Soc. Health, 121, 177-184.

C9. Brundrett, G. (2001). Comfort and health in commercial aircraft: a literature review. J. R. Soc. Health, 121, 29-37.

C10. Caldwell, J.A. (2001). The impact of fatigue in air medical and other types of operations: a review of fatigue facts and potential countermeasures. Air Med. J., 20, 25-32.

C11. Rayman, B. (2001). Aircraft cabin air quality: an overview. Uchu Koku Kankyo Igaku, 38, 9-15.

C12. Backman, H., Haghighat, F. (2000). Air quality and ocular discomfort aboard commercial aircraft. Optometry, 71, 653-656.

C13. Bowles, S., Ursin, H., Picano, J. (2000). Aircrew perceived stress: examining crew performance, crew position and captains personality. Aviat. Space Envioron. Med., 71, 1093-1097.

C14. Cho, K., Ennaceur, A., Cole, J.C., Suh, C.K. (2000). Chronic jet lag produces cognitive deficits. J. Neurosci., 20, RC66.

C15. Aspholm, R., Lindbohm, M.L., Paakkulainen, H. et al. (1999). Spontaneous abortions amongst Finnish flight attendants. J. Occup. Environ. Med., 41, 486-491.

C16. Rayman, R.B. (1997). Passenger safety, health and comfort: a review. Aviat. Space Environ. Med., 68, 432-440.

C17. Enck, P., Muller-Sacks, E. Holtmann, G., Wegmann, H. (1995). Gastrointestinal problems in airline crew members. Z. Gastroenterol., 33, 513-516.

C18. Shaner, S., Brooks, C., Osborn, R. et al. (1995). Flight crew physical fitness: a baseline analysis. Air Med. J., 14, 30-32.

C19. Haugli, L., Skogstad, A., Hellesoy, O.H. (1994). Health, sleep, and mood perceptions reported by airline crews flying short and long hauls. Aviat. Space Envioron. Med., 65, 27-34.

C20. Buja, A., Mastrangelo, G., Perissinotto, E. et al. (2006). Cancer incidence among female flight attendants: a meta-analysis of published data. J. Womens Health (Larchmt), 15, 98-105.

C21. Langner, I., Blettner, M., Gundestrup, M. (2004). Cosmic radiation and cancer mortality among airline pilots: results from a European cohort study (ESCAPE). Radiat. Environ. Biophys., 42, 247-256.

C22. Blettner, M., Zeeb, H., Auvinen, A. et al. (2003). Mortality from cancer and other causes among male airline cockpit crew in Europe. Int. J. Cancer, 106, 946-952.

C23. Irgens, A., Irgens, L.M., Reitan, J.B. (2003). Pregnancy outcome among offspring of airline pilots and cabin attendants. Scand. J. Work Environ. Health, 29, 94-99.

C24. Linnersjo, A., Hammar, N., Dammstrom, B.G. et al. (2003). Cancer incidence in airline cabin crew: experience from Sweden. Occup. Environ. Med., 60, 810-814.

C25. Paridou, A., Velonakis, E., Langner, I. et al. (2003). Mortality among pilots and cabin crew in Greece, 1960-1997. Int. J. Epidemiol., 32, 244-247.

C26. Pukkala, E., Aspholm, R., Auvinen, A. et al. (2003). Cancer incidence among 10,211 airline pilots: a Nordic study. Aviat. Space Environ. Med., 74, 699-706.

C27. Zeeb, H. Blettner, M., Langner, I. et al. (2003). Mortality from cancer and other causes among airline cabin attendants in Europe: a collaborative cohort study in eight countries. Am. J. Epidemiol., 158, 35-46.

C28. Zeeb, H., Langner, I., Blettner, M. (2003). Cardiovascular mortality of cockpit crew in Germany: cohort study. Z. Kardiol.,92, 483-489.

C29. Ballard, T.J., Lagorio, S., De Santis, M. (2002). A retrospective cohort mortality study of Italian commercial airline cockpit crew and cabin attendants, 1965-96. Int. J. Occup. Environ. Health. 8, 87-96.

C30. Blettner, M., Zeeb, H., Langner, I. et al. (2002). Mortality from cancer and other causes among airline cabin attendants in Germany, 1960-1997. Am. J. Epidemiol., 156, 556-565.

C31. Haldorsen, T., Reitan, J.B., Tveten, U. (2002). Aircraft accidents and other causes of death among Norwegian commercial pilots. Aviat. Space Environ. Med., 73, 587-592.

C32. Hammar, N., Linnersjo, A., Alfredsson, L. et al. (2002). Cancer incidence in airline and military pilots in Sweden 1961-1996. Aviat. Space Environ. Med., 73, 2-7.

C33. Zeeb, H., Blettner, M., Hammer, G.P., Langner, I. (2002). Cohort mortality study of German cockpit crew, 1960-1997. Epidemiology, 136, 693-699.

C34. Haldorsen, T., Reitan, J.B., Tveten, U. (2001). Cancer incidence among Norwegian airline cabin attendants. Int. J. Epidemiol., 30, 825-830.

C35. Rafnsson, V., Tulinius, H., Jonasson, J.G., Hrafnkelsson, J. (2001). Risk of breast cancer in female flight attendants: a population-based study (Iceland). Cancer Causes Control. 12, 95-101.

C36. Haldorsen, T., Reitan, J.B., Tveten, U. (2000). Cancer incidence among Norwegian airline pilots. Scand. J. Work Environ. Health, 26, 106-111.

C37. Rafnsson, V., Hrafnkelsson, J., Tulinius, H. (2000). Incidence of cancer among commercial airline pilots. Occup. Environ. Med., 57, 175-179.

C38. Gundestrup, M., Storm, H.H. (1999). Radiation-induced acute myeloid leukaemia and other cancers in commercial jet cockpit crew: a population-based cohort study. Lancet, 354, 2029-2031.

C39. Irvine, D., Davies, D.M. (1999). British Airways flightdeck mortality study, 1950-1992. Aviat. Space Environ. Med., 70, 548-555.

C40. Band, P.R., Le, N.D., Fang, R. et al. (1996). Cohort study of Air Canada pilots: mortality, cancer incidence, and leukemia risk. Am. J. Epidemiol.,143, 137-143.

C41. Pukkala, E., Auvinen, A., Wahlberg, G. (1995). Incidence of cancer among Finnish airline cabin attendants, 1967-92. BMJ, 311, 649-652.

C42. Band, P.R., Spinelli, J.J., Ng, V.T. et al. (1990). Mortality and cancer incidence in a cohort of commercial airline pilots. Aviat. Space Environ. Med., 61, 299-302.

C43. Amr MM. (1999). Pesticide monitoring and its health problems in Egypt, a third world country. Toxicology letters, 107, 1-13.

C44. Aldridge JE, Seidler F, Meyer A, Thillai I and Sltokin TA (2003). Serotonergic systems targeted by developmental exposure to chlorpyrifos (CPF): effects during different critical periods. Environmental Health Perspectives, 111, 1736-1743.

C45. Bazylwiccz-Walczak B, Majczakowa W and Szymczak M (1999). Behavioural effects of occupational exposure to organophosphorous pesticides in female green house planting workers. Neurotoxicology, 20, 819-825.

C46. Daughtrey W, Biles R, Jortner B and Ehrlich M (1996). Subchronic delayed neurotoxicity evaluation of Jet engine lubricants containing phosphorous additives. Fundamental Applied Toxicology, 32, 244-249.

C47. Delgado E, McConnell R, Miranda J, Keifer M, Lundberg I, Partanen T, Wesseling C (2004). Central nervous system effects of acute organophosphate poisoning in a two year follow up. Scan J Work E Health, 30, 362-370.

C48. Freudenthal RI, Rausch L, Gerhart JM, Barth ML, Mackerer CR and Bisinger EC. (1993). Subchronic neurotoxicity of oil formulations containing either tricresyl phosphate or tri-orthocresyl phosphate. J of Am College of Toxicology, 12, 409-416.

C49. Garcia SJ, Seidler FJ, Crumpton TL and Slotkin TA. (2001). Does the developmental neurotoxicity of chlorpyrifos involve glial targets? Macromolecule synthesis, adenyl cyclase signalling, nuclear transcription factors, and formation of reactive oxygen in C6 glioma cells. Brain Research, 891, 54-68.

C50. Jamal G, Hansen S, Ecne FA, Ecne AP, Abdul-Aziz M and Ballantyne JP (2001). Peripheral Nerve dysfunction in farmers using organophosphate sheep dip. J of Nutritional and Environmental Medicine, 11, 9-22.

C51. Kasa J Koupilova M and Vachek (2001). The influence of low-level sarin inhalation exposure on spatial memory in rats. Pharmacology Biochemistry and behaviour, 70, 175-179.

C52. Nishiwaki Y, Maekawa K, Ogawa Y, Asukai N, Minami M, Omae K, and Sarin health Effects Stdy Group. (2001). Effects of sarin on the nervous system in rescue team staff members and police officers 3 years after the Tokyo Subway sarin attack. Environmental Health Perspectives, 109, 1169-1173.

C53. Singh S and Sharma N (2000). Neurological syndromes following organophosphate poisoning. Neurology, India, 48, 308-313.

C54. Socko R, Gralewicz and Gorny R (1999). Long-term behavioural effects of a repeated exposure to chlorphenvinphos in rats. International Journal of Occupational Medicine and Environmental Health, 12, 105-117.

C55. Srivastava AK, Gupta BN, Bihari V, Mathur N, Srivastava LP, Pangtey BS, Bharti RS, and Kumar P. (2000). Clinical Biochemical and Neurobehavioural Studies of workers engaged in the manufacture of quinalphos. Food Chem Tox, 38, 65-69.

C56. Nagda N et al. Investigation of cabin air quality aboard commercial airlines. Indoor air 90. 5th International Conference on Indoor Air Quality and Climate. (Toronto 29 July 1990): 245-250.

C57. O'Donnell A et al (1991). Air quality, ventilation, temperature and humidity in aircraft. ASHRAE Journal 33, 42-6.

C58. Nagda N et al (1992). Measurement of cabin air quality aboard commercial airliners. Atmospheric Environment 26A: 2203-2210.

C59. Nagda N et al (1993). Cabin air quality aboard commercial airliners. Air and Waste Management Association 34: 243-248.

C60. Martinac I (1996). Cabin air quality (CAQ) onboard commercial jet aircraft. Proceedings of 14th International Congress on Biometrology, 1-8 September 1996, Slovenia.

C61. Dechow M et al (1997). Concentrations of selected contaminants in cabin air of airbus aircraft. Chemosphere 35: 21-31.

C62. Pierce M et al (1999). Air quality on commercial aircraft. AHSRAE Journal, 41: 26-34.

C63. Lee SC et al (1999). Indoor air quality investigation on commercial aircraft. Indoor Air, 9: 180-187.

C64. Hocking MB (2000). Passenger aircraft cabin air quality: trends, effects, societal costs, proposals. Chemosphere 41: 603-615.

C65. Lees SC et al (2000). Air quality measurements on sixteen commercial aircraft. In Air Quality and Comfort in Airliner Cabins, ASTM STP 1393, ed Nagda NL, American Society for Testing and Materials, West Conshohocken PA, 2000, pp45-55.

C66. Fox RB (2000). Air quality and comfort measurement aboard a commuter aircraft and solutions to improve perceived occupant comfort levels. In Air Quality and Comfort in Airliner Cabins, ASTM STP 1393, ed Nagda NL, American Society for Testing and Materials, West Conshohocken PA, 2000, pp161-183.

C67. Nagda NL et al. (2000). Aircraft cabin air quality: a critical review of past monitoring studies. In Air Quality and Comfort in Airliner Cabins, ASTM STP 1393, ed Nagda NL, American Society for testing and Materials, West Conshohocken PA, 2000, pp 215-235.

C68. Nagda NL et al. Determine aircraft supply air contaminants in the engine bleed air supply system on commercial aircraft. ENERGEN report AS20151, Project 959-RP, March 2001.

C69. Lindgren T and Norback D (2002). Cabin air quality: indoor pollutants and climate during intercontinental flights with and without tobacco smoking. Indoor Air 12: 263-272.

C70. Rayman RB (2002). Cabin air quality: an overview. Aviat Space Environ Med. 73: 211-5.

C71. Nagda NL and Rector HE (2003). A critical review of reported air concentrations of organic compounds in aircraft cabins. Indoor Air 13: 292-301.

C72. BRE. Extending cabin air measurements to include older aircraft utilised in high volume short haul operation. BRE Client Report 212034 prepared for Department of Health, October 2003.

C73. Phillips WD (2006). The high temperature degradation of hydraulic oils and fluids. Journal of Synthetic Lubrication 23: 39-70.

C74. Crane CR et al. (1983). Inhalation Toxicology II Evaluation of thermal degradation products from aircraft and automobile engine oils, aircraft hydraulic fluid, and mineral oil. Civil Aeromedical Institute, Federal Aviation Administration, Oklahoma City, Oklahoma. April 1983. FAA-AM-83-12.

C75. Anon. Study of possible effects on health of aircraft cabin environments-Stage2.

C76. BRE. Air quality monitoring in Boeing 757 aircraft. BRE Client Report 205923, 2001.

C77. Lipscomb J et al. Inhalation toxicity of vapour phase lubricants. US Air Force, Armstrong Laboratory, AL/OE-TR-1997-0090.

C78. Lhomme V et al. (1984). Thermal behaviour of some organic phosphates. Ind. Eng. Chem. Prod. Res. Dev. 23: 98-102.

C79. Paciorek et al (1978). Thermal oxidative degradation studies of phosphate esters. Am. Ind. Hyg. Assoc. J. 39: 633-639.

C80. Commetto-Muniz JE and Hernandez SM (1990). Odorous and pungent attributes of mixed and unmixed odourants. Perception and Psychophysics, 47, 391-399.

C81. Commetto-Muniz JE and Cain WS. (1992). Sensory irritation in relation to indoor air pollution. Ann New York Academy of Science, 641, 137-151.

C82. Schaper M (1993). Development of a database for sensory irritants and its use in establishing occupational exposure limits. American Industrial Hygiene Association Journal, 54, 488-544.

C83. Alarie Y, Schaper M, Nielsen GD and Abraham MH (1996). Estimating the sensory irritating potency of airborne nonreactive volatile organic chemicals and their mixtures. SAR and QSAR in Environmental Research, 5, 151-165, 1996.

C84. Cometto-Muniz JE, Cain WS, Abraham MH and Gola JMR (2001). Ocular and nasal trigeminal detection of butyl acetate and toluene presented singly and in mixtures. Toxicological Science, 63, 233-244.

C85. Shusterman D (2002). Individual factors in nasal chemesthesis. Chemical Senses, 27, 551-364.

C86. Kane LE and Alarie Y (1978). Evaluation of sensory irritation of acrolein-formaldehyde mixtures. American Industrial Hygiene Association Journal, 39, 270-274.

C87. Abraham MH, Nielesn GD and Alarie Y (1994). The Ferguson principle of biological activity of gases and vapours. J. Pharmaceutical Sciences, 83, 680-688.

C88. Alarie Y, Schaper M, Nielsen GD and Abraham MH (1998). Structure-activity relationships of volatile organic chemicals as sensory irritants. Archives of Toxicology, 72, 125-140.

C89. Kasanen JP, Pasanen AL, Pasanen P, Liesivuori J Kosma VM and Alarie Y (1998). Stereospecificity of the sensory irritation receptor for nonreactive chemicals illustrated by pinene enantiomers. Archives of Toxicology, 72, 514-523.

C90. Alarie Y (1998). Computer-based bioassay for evaluation of sensory irritation of airborne chemicals and its limits of detection. Archives of Toxicology, 72, 277-282.

C91. Damgard Nielsen G, Hougaard KS, Larsen ST, Hammer M, Wolkof P, Clausen PA, Wilkins CK and Alarie Y (1999). Acute airways effects of formaldehyde and ozone on BALB/c mice. Human and Experimental Toxicology, 18, 400-409.

C92. Muller WJ and Schaeffer VH (1996). A strategy for the evaluation of sensory and pulmonary irritation due to chemical emissions from indoor sources. J. Air and Waste Management Association, 46, 808-812.

C93. Luan F, Ma W, Zhang X, Zhang H, Liu M, Hu Z and Fan BT (2006). Quantitative structure-activity relationship models for prediction of sensory irritants (log RD_{50}) of volatile organic chemicals. Chemosphere, 63, 1142-1153.

C94. Cassee FR, Arts JHE, Groten JP and Feron VJ (1996). Sensory irritation to mixtures of formaldehyde, acrolein and acetaldehyde in rats. Archives of Toxicology, 70, 329-337.

C95. Kasanen JP, Pasanene AL, Pasanene P, Liesviuori J, Kosma VM and Alarie Y (1999). Evaluation of sensory irritation of Δ^3-careen and turpentine and acceptable levels of monoturpenes in occupational and indoor environment. J. Toxicology and Environmental Health, part A, 56, 89-114.

C96. Boylstein LA, Anderson SJ, Thompson RD and Alarie Y (1995). Characterisation of the effects of an airborne mixture of chemical on the respiratory tract and smoothing polynomial spline analysis of the data. Archives of Toxicology, 69, 579-589.

C97. Shusterman D, Makavinovic E and Salman A (2006). Does Haber's law apply to human sensory irritation? Inhalation Toxicology, 18, 457-471.

C98. Shusterman D, Murphy MA and Balmes J (2003). Differences in nasal irritatant sensitivity by age, gender, and allergic rhinitis status. International Archives of Occupational and Environmental Health, 76, 577-583.

C99. Abraham MH, Andonian-Haftvan J, Cometto-Muniz JE and Cain WS (1996). An analysis of nasal irritation threshold using a new solvation equation. Fundamental and Applied Toxicology, 31, 71-76.

C100. Cometto-Muniz JE, Cain WS, and Hudnell HK (1997). Agonistic sensory effects of airborne chemicals in mixtures: doors, nasal pungency and eye irritancy. Perception and Psychophysics, 59, 665-674.

C101. Cometto-Muniz JE, Cain WS, Hirashi T, Abraham MH, Gola JM (2000). Comparison of two stimulus-delivery systems for measurement of nasal pungency threshold. Chemical Senses, 25, 285-91.

C102. Hempel-Jorgensesn, Kjaergaard SK, Moljave L and Hudnell KH (1999). Sensory eye irritation in humans exposed to mixtures of volatile organic compounds. Archives of Environmental Health, 54, 416-424
.
C103. Walker JC, Kendal-Reed M, Utell MJ and Cain WS (2001). Human breathing and eye blink rate responses to airborne chemicals. Environmental Health Perspectives, 109, 507-512.

C104. Hempel-Jorgensen A, Kjaergaard SK and Molhave L (1998). Cytological changes and conjunctival hyperemia in relation to sensory eye irritation. International Archives of Occupational and Environmental Health, 71, 225-235.

C105. Cain WS, Lee NS, Wise PM, Schmidt R, Ahn BH, Cometto-Muniz JE, Abraham MH (2006). Chemesthesis from volatile organic compounds: psychophysical and neural responses. Physiology and Behaviour, 88, 317-324.

C106. Cometto-Muniz JE, Cain WS, Abraham MH and Kumarsingh R (1998). Sensory properties of selected terpenes. Thresholds for odor, nasal pungency, nasal localisation and eye irritation. Annals of New York Academy of Science, 855, 648-651.

C107. Cometto-Muniz JE, Cain WS, and Abraham MH (1998). Nasal pungency and odor of homologous aldehydes and carboxylic acids. Experimental Brain Research, 118, 180-188.

C108. Dalton P, Wysocki CJ, Brody MJ and Lawley HJ (1997). The influence of cognitive bias on the perceived odor, irritation and health symptoms from chemical exposure. International Archives of Occupational and Environmental Health, 69, 407-417.

C109. Cometto-Muniz JE, Cain WS (1995). Relative sensitivity of the ocular trigeminal, nasal trigeminal and olfactory systems to airborne chemicals. Chemical Senses, 20, 191-198.

C110. Abraham MH, Gola JMR, Kumarsingh R, Cometto-Miniz JE and Cain WS (2000). Connection between chromatographic data and biological data. Journal of Chromatography B, 745, 103-115.

C111. Abraham MH, Kumarsingh R, Cometto-Muniz JE and Cain WS. (1998). An algorithm for nasal pungency thresholds in man. Archives of Toxicology, 72, 227-232.

C112. Hau KM, Connell DW and Richardson BJ (1999). Quantitative structure-activity relationships for nasal pungency thresholds of volatile organic compounds. Toxicological Science, 47, 93-98.

C113. Cometto-Muniz JE, Cain WS and Abraham MH (2005). Determinants for nasal trigeminal detection of volatile organic compounds. Chemical Senses, 30, 627-642.

C114. Cometto-Muniz JE, Cain WS and Abraham MH (2005). Molecular restrictions for human eye irritation by chemical vapours. Toxicology and Applied pharmacology, 207, 232-243.

C115. Abraham M, Kumarsingh R, Cometto-Muniz JE, Cain WS (1998). Draize eye scores and eye irritation thresholds in man can be combined into one QSAR. Ann N Y Acad. Sci., 855, 652-6.

C116. Cometto-Muniz JE, Cain WS, Abraham MH and Gola JMR (1999). Chemosensory detectability of 1-butanol and 2-heptanone single and in binary mixtures. Physiology and Behaviour, 67, 269-276.

C117. Cometto-Muniz JE, Cain WS, Abraham MH and Gola JR (2001). Ocular and nasal trigeminal detection of butyl acetate and toluene presented singly and in mixtures. Toxicological Science, 63, 233-244.

C118. Cometto-Muniz JE and Cain WS and Abraham MH (2003). Dose-addition of individual odorants in the odor detection of binary mixtures. Behavioural Brain Research, 138, 95-103.

C119. Cometto-Muniz JE, Cain WS and Abraham MH (2004). Detection of single and mixed VOCs by smell and by sensory irritation. Indoor Air, 14 (suppl 8), 108-117.

C120. Cometto-Muniz JE, Cain WS and Abraham MH (2004). Chemosensory additivity in trigeminal chemoreception as reflected by detection of mixtures. Experimental Brain Research, 158, 196-206.

C121. Cometto-Muniz JE, Cain WS and Abraham MH (2005). Odour detection of single chemicals and binary mixtures. Behavioural Brain Research, 156, 115-123.

C122. Nielsen GD, Wolkoff P and Alarie Y (2007). Sensory irritation: risk assessment approaches. Regulatory Toxicology and Pharmacology, advance publication in e-format.

C123. Department of the Environment (1994). Expert panel on Air Quality Standards. Carbon monoxide. London HMSO.

C124. WHO Environmental health Criteria 213 (1999): Carbon Monoxide, 2nd edition, Finland, World Health organisation.

C125. Townsend CL and Maynard RL (2002). Effects on health of prolonged exposure to low concentrations of carbon monoxide. Occupational and Environmental Medicine, 59, 708-711.

C126. Department of Health (2004). Committee on Medical Effects of Air Pollutants. Guidance on the Effects on Health of indoor Air Pollutants, December pp1-54.

C127. Ryan JJ and Schnakenberg-Ott SD (2003). Scoring reliability on the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III). Assessment, 10(2),151-159.

C128. Lindgren T, Andersson K, Norback D (2006). Perception of cockpit environment among pilots on commercial aircraft. Aviat. Space Environ. Med., 77(8), 832-837.

C129. Lindgren T, Andersson K, Dammstrom BG, Norback D (2002). Ocular, nasal, dermal and general symptoms among commercial airline crews. Int. Arch. Occup. Environ. Health, 75(7), 475-483.

C130. Lindgren T, Norback D, Andersson K, Dammstrom BG (2000). Cabin environment and perception of cabin air quality among commercial aircrew. Aviat. Space Environ. Med., 71, 774-782.

C131. Lindgren T, Norback D, Andersson K, Dammstrom BG (1999). Subjective air quality, cabin air quality, and medical symptoms in aircrew. Indoor Air '99, 4, 1001-1006.

C132. Nicholas JS, Butler GC, Lackland DT et al. (2001). Health among commercial airplane pilots. Aviat. Space Environ. Med., 72(9), 821-826.

C133. Whelan EA, Lawson CC, Grajewski B, et al. (2003). Prevalence of respiratory symptoms among female flight attendants and teachers. Occup. Environ. Med., 60(12), 929-934.

C134. Ballard TJ, Romito P, Lauria L, et al. (2006). Self perceived health and mental health among women flight attendants. Occup. Environ. Med., 63(1):33-38.

C135. Cone JE (1984). Cabin air casualties: A flight attendant health survey. Report. Washington, DC: San Francisco General Hospital.

C136. de Ree H, Bagshaw M, Simons R, Brown RA (2000). Ozone and relative humidity in airline cabins on polar routes: measurements and physical symptoms. In: Air quality and Comfort in Airliner Cabins; Nagda NL, ed; ASTM STP 1393, West Conshohocken, PA.

C137. Eng WG (1979). Survey of eye comfort in aircraft: I. Flight attendants. Aviat. Space Environ. Med., 50, 401-404.

C138. Lee SC, Poon CS, Li XD et al. (2000). Questionnaire survey to evaluate the health and comfort of cabin crew. In: Air quality and Comfort in Airliner Cabins; Nagda NL, ed; ASTM STP 1393, West Conshohocken, PA.

C139. MacDonald LA, Deddens JA, Grajewski BA et al (2003). Job stress among female flight attendants. J. Occup. Environ. Med., 45(7), 703-714.

C140. McCarty DJ, McCarty CA. (2000). Survey of dry eye symptoms in Australian pilots. Clin. Exp. Ophthalmol., 28(3), 169-171.

C141. Norback D, Lindgren T, Wieslander G. (2006). Changes in ocular and nasal signs and symptoms among air crew in relation to air humidification on intercontinental flights. Scand. J. Work Environ. Health, 32(2), 138-144.

C142. Reed D, Glaser S, Kaldor J (1980). Ozone toxicity symptoms among flight attendants. Am. J. Ind. Med., 1(1), 43-54.

C143. Samel A, Wegmann HM, Vejvoda M (1997). Aircrew fatigue in long-haul operations. Accid. Anal. Prev., 29(4), 439-452.

C144. Spicer CW, Murphy MJ, Holdren MW et al. (2004). Relate air quality and other factors to comfort and health related symptoms reported by passengers and crew on commercial transport aircraft (Part 1). Report. Prepared by Batelle Science and Technology International. Prepared for ASHRAE, ASHRAE Project 1262-TRP, July.

C145. Tashkin DP, Coulson AH, Simmons MS, Spivey GH (1983). Respiratory symptoms of flight attendants during high altitude flight: Possible relation to cabin ozone exposure. Arch. Occup. Environ. Health, 52, 117-137.

C146. Wieslander G, Lindgren T, Norback D, Venge P (2000). Changes in the ocular and nasal signs and symptoms of aircrews in relation to the ban on smoking on intercontinental flights. Scand. J. Work Environ. Health, 26(6), 514-522.

C147. Kilburn KH (2004). Effects of onboard insecticide use on airline flight attendants. Arch. Environ. Health, 59(6), 284-291.

C148. California Health and Human Services Agency (2003). Occupational illness among flight attendants due to aircraft disinsection. Report. October 23.

C149. Martin-Saint-Laurent A, Lavernhe J, Casano G, Simkoff A (1990). Clinical aspects of inflight incapacitations in commercial aviation. Aviat. Space Environ. Med., 61(3), 256-260.

C150. Rayman RB (1973). Sudden incapacitation in flight, 1 Jan. 1966-30 Nov. 1971. Aerosp. Med., 44(8), 953-955.

C151. Australian Transport Safety Bureau (2003). BAe 146-100, VH-NJR, Occurrence: 200203243, 22 July 2002. Aviation Safety Investigation Report, Final, 8 May.

C152. Aviation Organo-phosphate Information Site (2003). Acknowledged odour occurrences. On-line compilation, March.

C153. Holland RB (1992). Air quality on long flights. Med. J. Aust., 157(6), 429.

C154. Porter HO (1990). Aviators intoxicated by inhalation of JP-5 fuel vapors. Aviat. Space Environ. Med., 61(7), 654-656.

C155. United States, National Institute for Occupational Safety and Health (1993). Alaska Airlines, MD80. Health Hazard Evaluation Report, HETA 90-226-2281, January.

C156. Voge VM (1997). Possible aircrew intoxication caused by accidental release of RainBoe: a case report. Aviat. Space Environ. Med., 68(12), 1159-1160.

C157. Institute for Environment and Health, University of Leicester, UK (2001). A consultation on the possible effects on health, comfort, and safety of aircraft cabin environments. IEH Web Report W5.

C158. American Society of Heating, Refrigerating, and Air-Conditioning Engineers (1999). Relate air quality and other factors to symptoms reported by passengers and crew on commercial transport aircraft. Final Report, ASHRAE/Consolidated Services, February.

C159. Marrison C, Muir H (1988). Cabin staff's perception of the impact of flying on their physical health. Aviat. Med. Quart., 2:11-17.

C160. Smolensky MH, Lee E, Mott D, Colligan M (1982). A health profile of American flight attendants. J. Human Ergol., 11(Suppl):103-119.

C161. Wieslander G, Norback D, Lindgren T (2001). Experimental exposure to propylene glycol mist in aviation emergency training: acute ocular and respiratory effects. Occup. Environ. Med., 58:649-655.

C162. House of Lords Select Sub-Committee on Science and Technology Fifth Report, November 2000.

C163. Institute for Environment and Health (IEH). A consultation on the possible effects on health, comfort and safety of aircraft cabin environments, March 2001.

C164. Unsolicited Data. Bleed air quality test fro LF502 engine S/N 5311. December 1999.

C165. Engineering investigation report. Customer bleed air testing engine model ALF502R-5 engine serial number LF05311. Honeywell International Inc.

C166. Test report air quality tests performed on BAe 146-200 aircraft registration number SE-DRE for the Swedish Board of Accident Investigation. Honeywell International Inc.

C167. Aaron DJ, Chang Y-F, Markovic N, LaPorte RE (2003). Estimating the lesbian population: a capture-recapture approach. J Epidemiol Community Health; 57(3): 207-209.

C168. Corrao G, Bagnardi V, Vittadini G, Favilli S (2000). Capture-recapture methods to size alcohol related problems in a population. J Epidemiol Community Health; 54(8): 603-610

C169. Smith RL, Smith T (2000). Ecology and Field Biology (ed: TM Smith), London: Addison Wesley.

C170. Wolkoff P et al, (2003). Eye irritation and environmental factors in the office environment- hypotheses, causes and a physiological model. Scand J Work Environ Health, 29, 411-30.

C171. Wolkoff P et al (2005). Eye complaints in the office environment: precorneal tear film (PTF) integrity influenced by eye blinking efficiency. Occupational and Environmental Medicine 62, 4-12.

C172. Wolkoff P et al (2006). Organic compounds in office environments – sensory irritation, odour, measurements and the role of reactive chemistry. Indoor Air, 16, 7-19.

C173. Wolkoff P et al (2006). The modern office environment desiccates the eyes? Indoor Air, 16, 258-265.

C174. Nojgaard JK et al (2005). The effect on human eye blink frequency of exposure to limonene oxidation products and methacrolein. Toxicol Letts, 156, 241-251.

C175. Wolkoff P and Kjaergaard SK. The dichotomy of relative humidity on indoor air quality. Accepted April 2007 for Environment International.

C176. Kleno J and Wolkoff P (2004). Changes in eye blink frequency as a measure of trigeminal stimulation by exposure to limonene oxidation products, isoprene oxidation products and nitrate radicals. Int Arch Occup Environ Health, 77, 235-243.

C177. Wilkins K et al. (2007). The impact of information on perceived air quality – 'organic' vs synthetic building materials. Indoor Air, 17, 130-134.