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Dear Professor Cranmer,

After careful review of the above paper and as a pilot and PhD holder on this very topic, with almost 20 years of direct research, [1,2] I consider there are many flaws with this article and I believe it ought to be withdrawn. I have listed just a few published studies that show why the views shown in this paper are inappropriate and I would be glad to write a more detailed paper on request.

The clear no effect position related to TOCP, can be partially understood in light of the conflict of interest with 4 of the 6 authors being paid by KLM in varying degrees, with it clearly unlikely the airline representatives will find a problem caused with the operation of their fleet. Indeed insurers would not allow liability to be acknowledged.

There is a clear reference to the one isomer of TCP, that is TOCP being linked to the “alleged” Aerotoxic Syndrome. This is quite disingenuous as 1) most papers make it clear that the cause of Aerotoxic Syndrome is related to the Triaryl phosphates (TAPs) including TCP, rather than simply TOCP, along with exposure to the ester base stock, pyrolysis substances and the antioxidant, PAN and its contaminants, that is the heated mixture. Those cited (Winder, Mackenzie Ross, Furlong & Abou-Donia), do not rely on TOCP as the potential causal factor with Aerotoxic Syndrome. While Furlong clearly refers to TAPs and TCP, Winder reported that “For TCP, the almost complete reliance on expressing TCP toxicity in terms of how much TOCP is present is misleadingly deceptive and ignores the possible contribution of other ingredients, some present in higher amounts and with appreciably higher toxicities.” [3]

The fact that TOCP has been referenced in a variety of studies and is therefore used as a suitable marker, [4] is unacceptable as it has clearly been known for many years that 1) TOCP is not the most toxic of the ortho isomers or the TAP mixture; 2) reliance on the TOCP levels, given the increased levels of the other ortho isomers, [5] underestimates the toxicity by a factor of over 30,000 times; [3] 3) there is no safe exposure level set for TCP and the exposure standard for TOCP cannot be used for TCP as a whole. [1,2,3,4,6,7,8] However this is still inappropriately common practice.

The other “ortho isomers” referenced in the oil at far higher levels than TOCP do not have standards and should not be so easily dismissed and of course TOCP is at such low level in the TAP blend [5] and is unlikely to be found.

The toxicological risk assessment based upon TOCP is poor quality science and shows a narrow understanding of what the literature and data reports on jet engine oil TAPs. To then suggest that Aerotoxic Syndrome is not related to the oil as the TOCP content is too low to cause toxic effects, is quite shocking and can be for 1 of 2 reasons alone: 1) protect the airline industry or 2) extremely poor understanding of the subject matter. To further suggest there may well be other reasons also shows a clear lack of understanding of the engineering principles of using a bleed air system, that based upon the use of pressurized air will and does allow low levels of oil leakage during normal monitoring and other studies.

As stated, to look at TCP alone and in particular TOCP, ignores the other TAP substances, of which there are many, the base stock, pyrolysis products and others. The Airbus worst case calculation of TOCP (0.025 mg/m3) exposure given to a House of Lords inquiry in the UK in 2000 clearly ignores all other isomers, other substances and the mixture.

To ignore the toxicity of the non ortho isomers is problematic as there is data to support that they are involved in inhibition of enzymes almost to the same extent as TOCP. [9] In 1954 it was found that that the non ortho isomers were involved with demyelination. [10] Likewise, DURAD 125, the commercial formulation of TCP used in engine oils has also been found to inhibit various enzymes, some of which are linked to cognition. [9]

Many other areas are problematic including:

- no inhalation toxicity studies for the oils have been undertaken [11,12] and it cannot be assumed that oral studies represent inhalation of a heated mixture.
- Inhalation is suggested to be the most efficient route of delivery for OPs to the nervous system, with dermal likewise reported to be more effective than oral and

12. ExxonMobil (2013)- letter from Frans B. Horjus, Global Aviation Lubricants Sales Manager for ExxonMobil Fuels & Lubricants to T Ellwood MP (UK), 24 may 2013
combined chemical exposures more efficient at causing nervous system injury than single exposures. [13]

- The common reliance upon the only effects of TOCP exposure being related to NTE inhibition & OPIDN ignores all other effects including inhibition of enzymes by other TAP isomers [9], other neurotoxic effects at very low levels [14] and OP induced neurotoxicity and chronic neurotoxicity. [13,15]
- The statement that exposure is far below the limit of 100,000 ng/m^3 is misleading as the exposure standard refers to TOCP alone, and has been found by ExxonMobil and others to be inapplicable for the other TCP isomers and inappropriately used. [1,2,3,4,6,7,8] Additionally ground based exposure standards should not be used in the aircraft environment or to complex mixtures and thermally decomposed products. [1,2,3,16,17]

The various studies show a consistent pattern of acute and chronic symptoms of dysfunction that can be clearly related to the working environment and identified contaminated air substances. The symptoms reported relate to a complex set of symptoms resulting from a unique occupational environment. While the specific symptoms can vary between people, the general types of symptoms are remarkably consistent. [1,2]

In summary it is worrying that a journal such as yours would rely upon a commercial entity, that cannot commercially identify a problem and in doing so relies upon an inappropriately narrow definition of toxicity related to one isomer of TCP alone and the one that is in the oil in the lowest quantity and therefore was always unlikely to be seen.

I trust this is useful information for you.

Sincerely,

Dr Susan Michaelis PhD, ATPL
Head of Research
GCAQE

16. ACGIH (2008) American Conference of Governmental Industrial Hygienists. TLVs and BEIs, Appendix E-Threshold limit values for mixtures & Appendix F- Minimal Oxygen Content. 2008