To: Mr. Richard Luit
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Centre for Safety of Substances and Products
RIVM
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Email: richard.luit@rivm.nl

Utrecht and Brussels, 14 October 2022

RE: Response to your letter VSP-2022-0026 regarding 2021 RIVM substance evaluation conclusion report of tris(methylphenyl) phosphate (TCP)

Dear Mr. Luit:

On behalf of the members of FNV, ETF, and GCAQE, we thank you for your letter dated 12 September 2022. We are collectively writing to you again because we continue to be deeply troubled by the ramifications of what we consider to be a significant disconnect between, on the one hand, the limited scope of RIVM's 2021 TCP neurotoxicity review and, on the other hand, its all-encompassing conclusions.

In your most recent letter, you described the scope, purpose, and conclusions of the RIVM substance evaluation for TCP dated 12 November 2021.[1] We have researched and understand the relevant REACH regulations, and we have read the RIVM report carefully from cover to cover. We raised our concerns with ECHA and your team in writing from December 2021 to April 2022 (Attachments 1-6) and we met with the RIVM team virtually on 15 July 2022 (Attachment 7). Still, our concerns remain unaddressed. Specifically, RIVM did not assess the "potential neurotoxic effects…of TCP as an additive in oils used in airplane engines and subsequent exposure of TCP or breakdown products to cabin crew, pilots, and passengers," despite that being part of the rationale (if not the primary reason) for ECHA to include TCPs on its 2011 list of 91 chemicals to review. To be clear, aircraft occupants *inhale* fumes that are generated when the engine oil (including its TCP additives) is exposed to *high temperatures* in the engine compressor, as previously described. Crews report chronic exposure to transient fumes (typically associated with engine power setting changes) that are

[1] ECHA. Substance evaluation conclusion as required by REACH Article 48 and Evaluation Report for Tris(methylphenyl) phosphate, EC No 809-930-9, CAS No 1330-78-5 (Previously registered as EC number215-548-8, CAS RN 1330-78-5). Report prepared by RIVM (National Institute for Public Health and the Environment), Bilthoven, The Netherlands, 12 November 2021. https://echa.europa.eu/documents/10162/25602787-d660-8be0-14c3-bcb7d2155f82

typically treated as "normal"; this type of routine, low-level exposure has been documented.[2-3] These exposures are sometimes punctuated by more sustained and apparently higher-level exposures which typically involve a reported odour, documented symptoms, and disruption to the flight.[4-5] Also of note, the fumes generated upon heating engine oils appear to be dominated by ultrafine particles.[6,7,8,9,10] Despite these typical fume event characteristics, your team appeared to review registrants' studies that described the potential neurotoxic effects of *ingesting* TCPs at *room temperature* that did not have the same trade name (and, thus, may be a different *isomeric blend*) as the TCPs in aviation engine oils. Also, the rats in the registrants' studies effectively ingested these droplet aerosols for *four uninterrupted weeks*. Four weeks in the life of an average rat is not "chronic" and the exposure pattern did not mimic that of airline crewmembers.

Also, your team did not follow through on its stated intention to address the *"as yet insufficient information in the dossier regarding the exposure of air cabin crew, pilots and passengers to TCP, or breakdown products, during intended use of TCP as additive in oils used in airplane engines."* [11] Instead, RIVM allowed the registrants to review the exposures and reported symptoms from a *dissimilar exposure group* (i.e., workers in a TCP production plant), with no information on either their job tasks or exposure potential.

Despite these significant differences and omissions, in Table 3 of the RIVM report, next to the text that reads *"Potential neurotoxic effects of the substance in aviation uses,"* it says, *"Concern refuted,"* and *"Sufficient information available for the eMSCA to evaluate the neurotoxicity. Concern not substantiated, no further action."* Also, under *"Exposure assessment,"* the report says, *"Sufficient information…to evaluate the exposure scenarios."* These conclusions are not supported by your review. In 2013, RIVM recognized that

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[2] Crump D; Harrison P; and Walton C. Aircraft cabin air sampling study: Part 1 and 2 of the final report. Cranfield: Institute of Environment and Health, Cranfield University; 2011. https://dspace.lib.cranfield.ac.uk/handle/1826/5305, https://dspace.lib.cranfield.ac.uk/handle/1826/5306.

[3] Airbus. A clean APU means clean cabin air. In: FAST (Flight Airworthiness Support Technology) 2013, 52: 4-9, Airbus SAS. Available online: https://perma.cc/ZK7P-JZ8V.

[4] Murawski, J. Case study: Analysis of reported contaminated air events at one major US airline in 2009–10, Paper ID: AIAA-2011-5089. Proc. 41st Intl Conf on Environ Sys, Am Inst Aeronaut Astronaut, 17–21 July 2011. Portland, Oregon. https://arc.aiaa.org/doi/10.2514/6.2011-5089.

[5] Michaelis, S; Burdon, J; Howard CV. Aerotoxic Syndrome: A new occupational disease? Public Health Panorama; 2017, 3: 198-211, World Health Organization, https://apps.who.int/iris/handle/10665/325308.

[6] Jones B; Roth J; Hosni M; et al. The nature of particulates in aircraft bleed air resulting from oil contamination. LV-17-C046. In: 2017 ASHRAE Winter Conference—Papers. American Society of Heating, Refrigerating, and Air Conditioning Engineers, Atlanta, Georgia, USA.

[7] Mann, GW; Eckels, SJ; and Jones, BW. Analysis of particulate size distribution and concentrations from simulated jet engine bleed air incidents. HVAC and R Research 2014, 20: 780-789, https://doi.org.10.1080/10789669.2014.950922.

[8] Michaelis, S; Loraine, T; and Howard, CV. Ultrafine particle levels measured on-board short-haul commercial passenger jet aircraft. Environmental Health 2021, 20(89): 1-14, https://doi.org.10.1186/s12940-021-00770-7.

[9] Nayyeri, S; Jones, B; and Hosni, M. Characterization of particulate resulting from oil contamination of aircraft bleed air. SAE Int. J. Aerosp, 2021, 14(1):45-62, https://doi.org/10.4271/01-14-01-0002.

[10] ASHRAE. Experimental characterization of aircraft bleed air particulate contamination, Final report, 1830-RP. Author: Jones, B. Submitted to the American Society of Heating Refrigerating and Air-Conditioning Engineers, TC9.3 Transportation Air Conditioning Committee, Atlanta, GA. March 2022.

[11] ECHA. "Justification for the selection of a candidate CoRAP substance: Tris(methylphenyl)phosphate, EC no. 215-548-8, CAS no. 1330-78-5; submitted by RIVM (NL-CA); published March 20, 2013 and updated March 26, 2014. https://echa.europa.eu/documents/10162/48963b43-6bfc-475d-1f05-8ff50a482a61.

crewmembers can inhale heated engine oils that contain TCPs and its byproducts, telling ECHA that *"[f]or human health, our primary concern relates to the potential neurotoxic effects of (isomers of) TCP, especially due the use of TCP as additive in oils used in airplane engines and subsequent exposure of TCP, or breakdown products, to cabin crew, pilots and passengers."* [11] We are left to wonder then, what changed? Table 3 in the RIVM report should simply state: "Insufficient information reviewed for the eMSCA to evaluate the neurotoxicity *of inhaling heated TCPs*," and "Insufficient information…to evaluate exposure scenarios involving *inhalation of heated TCPs.*" Such conclusions would appropriately reflect the review that RIVM undertook. The conclusory statements in section 7.9.11 of the RIVM report – as they relate to inhalation of heated TCPs and its byproducts - should also be amended accordingly.

Within days of our virtual meeting with you in July 2022, we emailed your team a series of slides that included a list of limitations that we asked to be acknowledged in the RIVM report (Attachment 7). Listing limitations is professional best practice, but three months have passed, and the only limitation listed in the report appears to be that *"histopathology section…could be more informative."* In your 12 September 2022 letter to us, you noted that your review did not cover *"complex by-products"* that are a result of heating TCPs in aviation engine oils. But how can you draw any conclusion about the potential neurotoxic effects to crewmembers who inhale TCPs sourced to an aircraft engine – whether TCPs are part of a chemical mixture or not - if the TCPs are not heated, such that the test conditions are irrelevant to crewmembers' workplace?

In your 12 September 2022 letter to us, you also seem to reassure us that *"[t]he conclusion on TCP does not discard any remaining concerns on potential health risks for pilots and cabin crew potentially caused by other substances released from heated turbine engine oils or on endpoints other than neurotoxicity."* We cannot accept this statement because your review did not assess the neurotoxic effects of exposure to heated TCPs for pilots and cabin crew.

Current data suggests that inhalation exposure to neurotoxic substances (in this case, TCPs), contributes to the types of neurological symptoms that crewmembers continue to document after a fume event. However, we do not consider TCPs to alone be responsible for the reported ill health; rather, with regards to TCPs, we consider that the combination of TCPs and other *"substituted phenols as well as xylenols, as well as low levels of ortho cresol and phenol in hydrolysed conventional TCP"*[12] as part of a complex mixture of an estimated 127 compounds,[13] all attached to ultrafine particles of a suitable size and solubility to travel to the brain directly through nerve pathways in the face and enter circulation after crossing the lung epithelium[14] to be the most likely explanation.

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[12] Mackerer, CR and Ladov, EN. Submission to the Senate References Committee, Rural and Regional Affairs and Transport on the Inquiry into Air Safety – Bae146 Cabin Air Quality, 1999, Submitted by Mobil Business Resources Inc., Paulsboro, New Jersey, USA. Available online: https://perma.cc/NQV6-UU6T.

[13] Houtzager, M; Noort, D; Joosen, M; et al. Characterisation of the toxicity of aviation turbine engine oils after pyrolysis (AVOIL); see Table 5.6. Project No. 923642/060.18709, 2017. Published by the European Aviation Safety Agency, Cologne, Germany. Available online at: https://www.easa.europa.eu/document-library/research-reports/easarepresea20152.

[14] Howard, CV; Johnson, DW; Morton, J; Michaelis, S; Supplee, D; and Burdon J. Is a cumulative exposure to a background aerosol of nanoparticles part of the causal mechanism of Aerotoxic Syndrome? 2018, J Nanomed Nanosci 2018; JNAN-139, https://perma.cc/2CU6-L7HN.

To conclude, despite our correspondence and meeting with you, we remain deeply troubled about your report. Taking the principles of good governance in mind, we ask you - as decision-makers - to thoroughly consider how your report is likely to be used outside the REACH process, and to ensure that its use is consistent with the legitimate expectations and needs of citizens. We understand that REACH requires you to consider all exposure scenarios but, given that crewmembers' reports of neurotoxicity were one of the main justifications for the neurotoxicity review, it does not make sense to exclude their exposure scenarios and then draw a sweeping conclusion that includes them. For this reason, we urge you to review the report and narrow the conclusions, as described. At a minimum, it is important that you describe the limitations of the registrants' data (as it applies to airline workers) to at least better enable readers to put your conclusions in context. This type of transparency and good faith is particularly important considering that, specific to engine oil fumes, RIVM is active in the regulatory arena (i.e., REACH) while it is also partners with the aviation industry in research (i.e., AVOIL, FACTS1, and CAQ3). Please respond to us by email at the addresses noted below.

Sincerely,

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CC: Dr. Sharon McGUINNESS, Executive Director, ECHA

Attachments:
1. Letter from ETF to ECHA, 10 December 2021
2. Letter from Prof. V. Howard and Dr. S. Michaelis to ECHA, 12 December 2021
3. Letter from T. Loraine/GCAQE to ECHA, 12 December 2021
4. Letter from Prof. V. Howard and Dr. S. Michaelis to RIVM, 24 January 2022
5. Letter from FNV and ETF to RIVM, 25 January 2022
6. Letter from FNV and ETF to RIVM, 27 April 2022
7. Slides from ETF/Michaelis/Howard with limitations sent to RIVM, 19 July 2022