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## **Supplemental Material**

## **Exposure to per- and Polyfluoroalkyl Substances and Markers of Liver Injury: A Systematic Review and Meta-Analysis**

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**References** 

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# **Description of domains in Office of Health Assessment and Translation (OHAT) Risk of Bias tool**







NR: not reported; EA: experimental animal study; Co: cohort study; CrSe: cross sectional study

## **Review articles screened for additional eligible articles**

Deierlein AL, Rock S, Park S. 2017. Persistent endocrine-disrupting chemicals and fatty liver disease. Current environmental health reports 4:439-449.

Fenton SE, Ducatman A, Boobis A, DeWitt JC, Lau C, Ng C, et al. 2021. Per- and polyfluoroalkyl substance toxicity and human health review: Current state of knowledge and strategies for informing future research. Environ Toxicol Chem 40:606-630.

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Legend: definitely low risk of bias (++); probably low risk of bias (+); probably high risk of bias (-); definitely high risk of bias (--); not reported (NR) Four elements did not apply to cross-sectional and cohort studies and were excluded from the table.









Legend: definitely low risk of bias (++); probably low risk of bias (+); probably high risk of bias (-); definitely high risk of bias (--); not reported (NR) Two elements did not apply to animal studies and were excluded from the table.

**Table S3.** Weighted Z-scores for the cross-sectional associations of PFAS with ALT and GGT in humans with selected exclusions.



Note: perfluoroalkyl substance (PFAS); alanine aminotransferase (ALT); gamma-glutamyl transferase (GGT); perfluorooctanoic acid (PFOA); perfluorooctane sulfonic acid (PFOS); National Health and Nutrition Examination Survey (NHANES)



**Table S4.** Weighted Z-scores for the cross-sectional associations of PFAS with GGT and AST in humans ≥ 12 years old.

Note: perfluoroalkyl substance (PFAS); gamma-glutamyl transferase (GGT); aspartate aminotransferase (AST); perfluorooctanoic acid (PFOA); perfluorooctane sulfonic acid (PFOS); perfluorononanoic acid (PFNA); perfluorohexane sulfonate (PFHxS)



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Figure S1. Strip plots for PFOA and AST in animal studies. Blue triangles indicate a significant increase in AST and red diamonds indicate a significant decrease in AST relative to control. Circles indicate no significant change in AST relative to control. Abbreviations: End of treatment (EOT); low fat diet (LFD); high fat diet (HFD); postnatal day (PND); gestational day (GD); embryonic day (E); Sprague Dawley (SD); 4-phenylbutyric acid (4-PBA); fasted (F); non-fasted (NF); concanavalin A (Con A); quecertin (Que); N-acetylcysteine (NAC); grape seed proanthocyanidin extract (GSPE). Additional exposures in Shi et al (2021) refer to lactic acid bacterial strains. An accessible version of this figure is available in Table S7.





Figure S2. Strip plots for PFOA and relative liver weight in animal studies. Blue triangles indicate a significant increase in relative liver weight relative to control. Circles indicate no significant change in relative liver weight relative to control. Plots are ordered by species and strain. Abbreviations: End of treatment (EOT); low fat diet (LFD); high fat diet (HFD); postnatal day (PND); gestational day (GD); embryonic day (E); Sprague Dawley (SD); *N-*acetylcysteine (NAC); 4-phenylbutyric acid (4-PBA). Additional exposures in Shi et al (2021) refer to lactic acid bacterial strains. An accessible version of this figure is available in Table S8.



**Figure S3.** Strip plots for PFOS and AST in animal studies. Blue triangles indicate a significant increase in AST and red diamonds indicate a significant decrease in AST relative to control. Circles indicate no significant change in AST relative to control. Plots are ordered by species and strain. Abbreviations: End of treatment (EOT); embryonic day (E); Vitamin C (VC); polychlorinated biphenyl (PCB); diethylnitrosamine (DEN); choline supplementation (CS); concanavalin A (Con A); naringin (Nar); Sprague Dawley (SD); grape seed proanthocyanidin extract (GSPE). An accessible version of this figure is available in Table S9. 0 40 80



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Figure S4. Strip plots for PFOS and relative liver weight in animal studies. Blue triangles indicate a significant increase in relative liver weight relative to control. Black dots indicate no significant change in relative liver weight relative to control. Plots are ordered by species and strain. Abbreviations: End of treatment (EOT); marginal methionine/choline-deficient diet (mMCD); choline supplementation (CS); naringin (Nar); Sprague Dawley (SD); grape seed proanthocyanidin extract (GSPE); high fat diet (HFD); low fat diet (LFD); initial high fat diet followed by standard diet (HFD/STD). \*Atmospheric exposure occurred for 5 hours/day, 5 days/week. An accessible version of this figure is available in Table S10.

# **Table S5. Results for PFOA and ALT in animal studies.**







## Notes:

*Abbreviations:* End of treatment (EOT); low fat diet (LFD); high fat diet (HFD); postnatal day (PND); gestational day (GD); embryonic day (E); Sprague Dawley (SD); N-acetylcysteine (NAC); 4-phenylbutyric acid (4-PBA); quecertin (Que); fasted (F); non-fasted (NF); grape seed proanthocyanidin extract (GSPE). Additional exposure abbreviations in Shi et al (2021) refer to lactic acid bacterial strains.

# **Table S6.** Results for PFOS and ALT in rodent studies.





## Notes:

*Abbreviations:* End of treatment (EOT); embryonic day (E); Vitamin C (VC); diethylnitrosamine (DEN); marginal methionine/choline-deficient diet (mMCD); choline supplementation (CS); concanavalin A (Con A); naringin (Nar); Sprague Dawley (SD); grape seed proanthocyanidin extract (GSPE). \*Atmospheric exposure occurred for 5 hours/day, 5 days/week.

# **Table S7. Results for PFOA and AST in animal studies.**





# Notes:

*Abbreviations:* End of treatment (EOT); low fat diet (LFD); high fat diet (HFD); postnatal day (PND); gestational day (GD); embryonic day (E); Sprague Dawley (SD); N-acetylcysteine (NAC); 4-phenylbutyric acid (4-PBA); quecertin (Que); fasted (F); non-fasted (NF); grape seed proanthocyanidin extract (GSPE). Additional exposure abbreviations in Shi et al (2021) refer to lactic acid bacterial strains.

# **Table S8. Results for PFOA and relative liver weight in animal studies.**







## Notes:

*Abbreviations:* End of treatment (EOT); low fat diet (LFD); high fat diet (HFD); postnatal day (PND); gestational day (GD); embryonic day (E); Sprague Dawley (SD); N-acetylcysteine (NAC); 4-phenylbutyric acid (4-PBA); quecertin (Que); grape seed proanthocyanidin extract (GSPE). Additional exposures in Shi et al (2021) refer to lactic acid bacterial strains.

# **Table S9. Results for PFOS and AST in animal studies.**





Notes:

Abbreviations: End of treatment (EOT); embryonic day (E); Vitamin C (VC); diethylnitrosamine (DEN); marginal methionine/choline-deficient diet (mMCD); choline supplementation (CS); concanavalin A (Con A); naringin (Nar); Sprague Dawley (SD); grape seed proanthocyanidin extract (GSPE). \*Atmospheric exposure occurred for 5 hours/day, 5 days/week.

# **Table S10. Results for PFOS and relative liver weight in animal studies.**







Notes:

Abbreviations: End of treatment (EOT); embryonic day (E); Vitamin C (VC); diethylnitrosamine (DEN); marginal methionine/choline-deficient diet (mMCD); choline supplementation (CS); concanavalin A (Con A); naringin (Nar); Sprague Dawley (SD); grape seed proanthocyanidin extract (GSPE). \*Atmospheric exposure occurred for 5 hours/day, 5 days/week.

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