

**From:** Joseph Cotruvo  
**Sent:** Wednesday, September 14, 2022 10:43 AM  
**To:** Brennan, Thomas <[Brennan.Thomas@epa.gov](mailto:Brennan.Thomas@epa.gov)>  
**Subject:** PFAS

Dr Brennan,

Please also post this very recent article regarding the weakness of using immunomodulation endpoints for risk assessment.

<https://cris.maastrichtuniversity.nl/en/publications/immunomodulation-and-exposure-to-per-and-polyfluoroalkyl-substanc>

Thanks

Joseph Cotruvo

## Immunomodulation and exposure to per- and polyfluoroalkyl substances: an overview of the current evidence from animal and human studies

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- [CAPHRI - Optimising Patient Care](#)
- [Epidemiologie](#)
- [NUTRIM - Respiratory & Age-related Health](#)

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### Abstract

Per- and polyfluoroalkyl substances (PFAS) have been widely used and represent a class of environmental persistent chemicals. An association of a reduction of vaccination efficacy with PFAS

serum levels in humans was used by the European Food Safety Authority as a key effect for PFAS risk assessment. The data support for using this association is reviewed by a critical analysis of the respective human epidemiology and the available animal studies on the immunomodulation of PFAS. Based on an analysis of the available human epidemiology, the overall level of evidence regarding associations between PFAS serum levels and reduced antibody response remains weak. Absence of an association between an increase in clinical infections and PFAS serum levels and the limited understanding of the importance of antibody levels as an isolated data point further support this conclusion. Animal toxicity studies with PFAS focusing on immunomodulation also provide only limited support for immunomodulation as an important endpoint in PFAS toxicity. While immunomodulation is observed after PFAS administration, generally at blood concentrations several orders of magnitude above those seen in environmentally exposed humans, the relevance of these observation is hampered by the high doses required to influence immune endpoints, the limited number of endpoints assessed, and inconsistent results. The limitations of the current database on associations of human PFAS exposures outlined here indicate that more evidence is required to select immunomodulation as a critical endpoint for human PFAS risk assessment.

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- SHORT-TERM EXPOSURE
- PRENATAL EXPOSURE
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