

# **NTP Monograph on Immunotoxicity Associated with Exposure to PFOA or PFOS**

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NTP Board of Scientific Counselors Meeting  
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# Exposure and Immune Effects

- **Perfluoroalkyl acids including PFOA and PFOS**

- Used extensively in commercial/industrial applications last 50 years
  - food packaging
  - water-resistant coatings
  - lubricants
  - fire-retarding foams



- **PFOA and PFOS**

- US production eliminated; use and emissions reduced in US and much of Europe through voluntary agreements
- Not metabolized or expected to degrade in environment

- **Reported immune effects of both PFOA and PFOS**

- Effects on antibody response in animals at some of lowest doses
- Recent studies reporting similar antibody effects in humans
- PFOA and PFOS appeared to share some effects and differ for others



# NTP Conducted A Systematic Review

- First OHAT evaluation to use OHAT Approach for Systematic Review and Evidence Integration to reach hazard conclusions
- **Objectives**
  - To develop NTP hazard identification conclusions on the association between exposure to PFOA or PFOS (or their salts) and immunotoxicity
  - Conclusions for each chemical were reached by integrating evidence from human and animal studies with consideration of the degree of support from mechanistic data



# Peer Review Panel Meeting

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- July 19, 2016 at NIEHS in Research Triangle Park, NC
- **Chair**
  - Weihsueh Chiu, PhD – Texas A&M University
- **Panel**
  - Joseph Braun, PhD – Brown University
  - Emanuela Corsini, PhD – Univeristita degli Sudi di Milano
  - Berit Granum, PhD – Norwegian Institute of Public Health
  - Deborah Keil, PhD, DABT – Montana State University
  - Michael Woolhiser, PhD – The Dow Chemical Company
- **BSC Liaison**
  - Paul Brandt-Rauf, DrPH, MD, ScD – University of Illinois at Chicago



# Charge to the Panel

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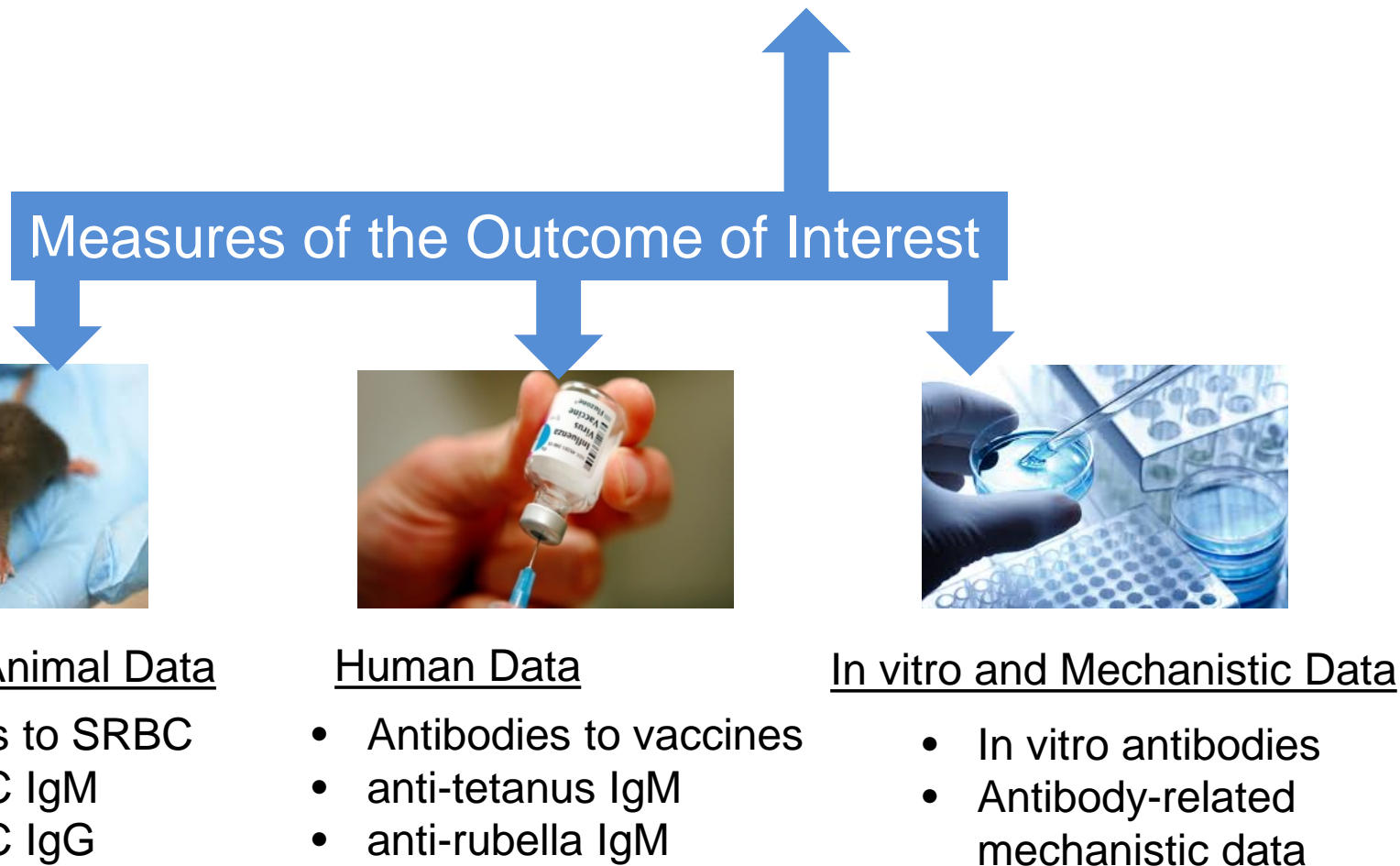
- To determine whether the scientific information cited in the draft monograph is technically correct and clearly stated, and whether NTP has objectively presented and assessed the scientific evidence.
- To determine whether the scientific evidence presented in the draft NTP monograph supports the NTP's conclusions regarding whether immunotoxicity is associated with exposure to PFOA or PFOS.



# Conclusions Based on Bodies of Evidence

## Results Grouped by Same or Related Outcomes

- **Primary outcomes:** Direct health outcomes or endpoints
  - **Example:** Immunosuppression - reduced antibody response

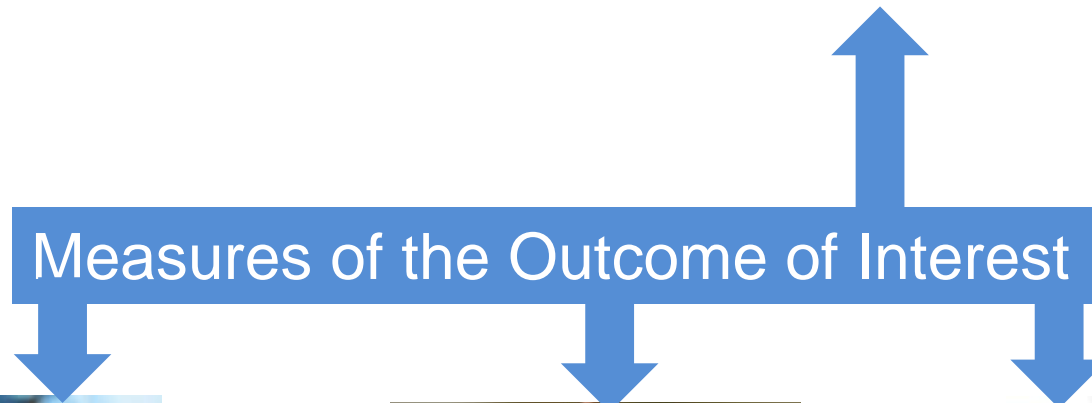




# Conclusions Based on Bodies of Evidence

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### Experimental Animal Data

- Antibodies to SRBC
- anti-SRBC IgM
- anti-SRBC IgG



### Human Data

- Antibodies to vaccines
- anti-tetanus IgM
- anti-rubella IgM



### In vitro and Mechanistic Data

- In vitro antibodies
- Antibody-related mechanistic data



# Draft Conclusions on PFOA Immunotoxicity

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- NTP conclusions are based on the highest level-of-evidence conclusions for immune effects on an outcome basis
- PFOA is **presumed to be an immune** hazard to humans based on two separate lines of evidence:
  - **(1) PFOA suppressed the antibody response**
    - Animal studies: High level of evidence
    - Human studies: Moderate level of evidence
    - No change in conclusions after considering mechanistic data
  - **(2) PFOA increased hypersensitivity-related outcomes**
    - Animal studies: High level of evidence
    - Human studies: Low level of evidence
    - No change in conclusions after considering mechanistic data





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The Panel accepted the level of evidence ratings for the antibody response data as written



# Draft Conclusions on PFOA Immunotoxicity

- NTP conclusions are based on the highest level-of-evidence conclusions for immune effects on an outcome basis
- PFOA is **presumed to be an immune hazard** to humans based on two separate lines of evidence :

- (1) PFOA suppressed the animal immune system
  - Animal studies: High level of evidence
  - Human studies: Moderate level of evidence
  - No change in conclusions after considering mechanistic data

The Panel concluded the level of evidence for the animal hypersensitivity-related data was Moderate

- Limited number of studies
- Divergent response to PFOA

- (2) PFOA increased hypersensitivity-related outcomes
  - Animal studies: ~~High~~ **Moderate** level of evidence
  - Human studies: Low level of evidence
  - No change in conclusions after considering mechanistic data



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- PFOA is **presumed to be an immune** hazard to humans based on two separate lines of evidence:

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- **(2) PFOA increased hypersensitivity-related outcomes**

- Animal studies: High level of evidence
- Human studies: Moderate level of evidence
- No change in conclusions after considering mechanistic data

*... after downgrading the hypersensitivity data*

The Panel accepted the hazard conclusion for PFOA based on the antibody response data



# Draft Conclusions on **PFOS** Immunotoxicity

- Similar evidence base for PFOS with the highest level-of-evidence conclusions for immune effects based on only the antibody response
- PFOS is **presumed to be an immune** hazard to humans based on:
  - **PFOS suppressed the antibody response**
    - Animal studies: High level of evidence
    - Human studies: Moderate level of evidence
    - No change in conclusions after considering mechanistic data

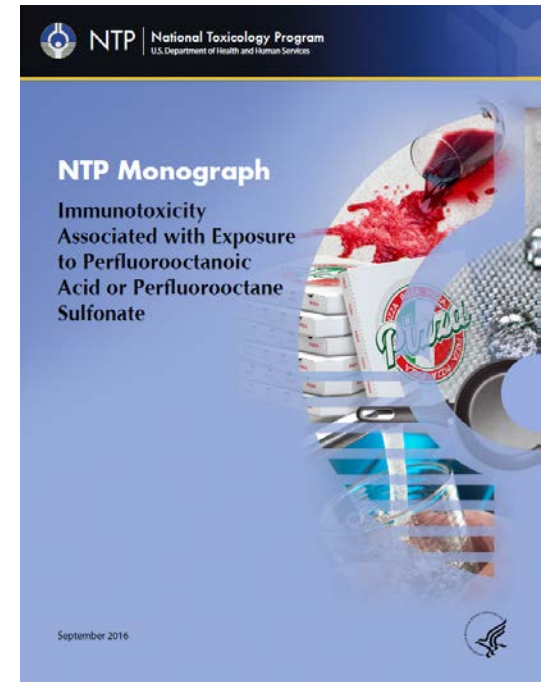


The Panel accepted the hazard conclusion for PFOS based on the antibody response data



# Final Conclusions on PFOA and PFOS

- Following the Peer-Review Meeting
  - Comments from the public and Peer-Review Panel were considered
  - **NTP Monograph** finalized (<http://ntp.niehs.nih.gov/go/749926>)
  - Studies, data, risk of bias, figures available (<https://hawcproject.org/assessment/57>)



- Conclusion - PFOA and PFOS are both ***presumed to be an immune hazard to humans***
  - Based on bodies of evidence that both chemicals suppressed the antibody response
    - High level of evidence from animal studies
    - Moderate level of evidence from human studies



Thank you