

**EXPOSOME +
GENOME = DISEASE**

NON-TARGETED ANALYSIS

**How many chemicals
are we exposed to?**



How many chemicals are we exposed to?

Environmental Topics

Laws & Regulations

About EPA

Critical period of development with unique susceptibility to biological/chemical perturbations

TSCA Chemical Substance Inventory

~80,000 chemical substances in total

~40,000 chemical substances actively used in the US

The inventory does not include

- Pesticides
- Food additives
- Drugs
- Cosmetics
- Tobacco products
- Nuclear materials
- Munitions



CompTox Chemicals Dashboard

883 Thousand Chemicals

Chemical manufacturers in the United States are allowed to self-regulate



Chemicals

Product/Use Categories

Assay/Gene

Q Search for chemical by systematic name, synonym, CAS number, DTXSID or InChIKey

Identifier substring search



A TODD HAYNES FILM

MARK
RUFFALO

ANNE
HATHAWAY

TIM
ROBBINS

BILL
CAMP

VICTOR
GARBER

AND
BILL
PULLMAN

DARK WATERS

ONE OF THE DEADLIEST COVER-UPS IN AMERICAN HISTORY

"A PERFECT FILM.
RIVETING, POWERFUL
AND IMPORTANT"
OBSERVER

"MARK RUFFALO'S
BEST PERFORMANCE YET"
HOLLYWOOD NEWS



Chemical manufacturers in the U.S. are allowed to “self-regulate”

THE DEVIL WE KNOW

THE CHEMISTRY OF A COVER-UP



Are there any
people not
exposed to
PFAS?





Program on Reproductive Health and the Environment @. · Feb 8 ...

#PFAS manufacturer @SolvayGroup blocked Wellington Labs from selling standards for a compound used to make fluoropolymers/PFAS. Another industry effort to prevent scientists from studying PFAS. @EPA must request analytical standards from manufacturers for all chemicals produced.

WELLINGTON
LABORATORIES

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January 27, 2021

Dear Valued Customer,

We apologize for the extended back-order that has been applied to our P5MeODIOXOAc product and regret to inform you that we are now discontinuing this product permanently. Wellington was notified in July of 2020 that the sale of our P5MeODIOXOAc standard for environmental testing and research (also known as C6O4, CAS 1190931-41-9) constituted an infringement of Solvay's patent rights. We were hoping to negotiate an arrangement with the patent holder that would facilitate the sale of this standard so that environmental analyses could continue; however, we were unable to come to an agreement that would allow for uncensored access to the standard. As such, Wellington must comply with Solvay's request to cease the production and sale of this certified



Ian Cousins @IanTCousins · Feb 8 ...

The US Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) requires manufactures of these products to make analytical standards available for their products and related metabolites. TSCA, which applies to all other chemical substances, has no such requirement.



1



3



23



Ian Cousins @IanTCousins · Feb 12 ...

An article about Solvay's attempts to impede research into their product.
#PFAS



Solvay Impedes Research Into Unknown PFAS by Threatening Testing...
Consumer Reports says Solvay impedes research into unknown PFAS by threatening a Canadian lab with legal action after claiming its pate...
[consumerreports.org](https://www.consumerreports.org)



Tracey Woodruff, PhD, MPH @TraceyJWoodruff · Feb 8 ...

#PFAS are a public health problem. Solvay Group is blocking access to a key tool for monitoring a replacement PFAS that could very likely be contaminating us and the environment.

@EPA needs to require analytic standards as part of TSCA



30 maternal blood samples

+

30 cord blood samples



Chemical analysis with high resolution mass spectrometry (HRMS)

Blood samples extraction
and clean-up



Analysis with LC –
QTOF/MS in
ESI+/- modes



Feature extraction and
alignment - Profinder



Formula assignment –
MPP

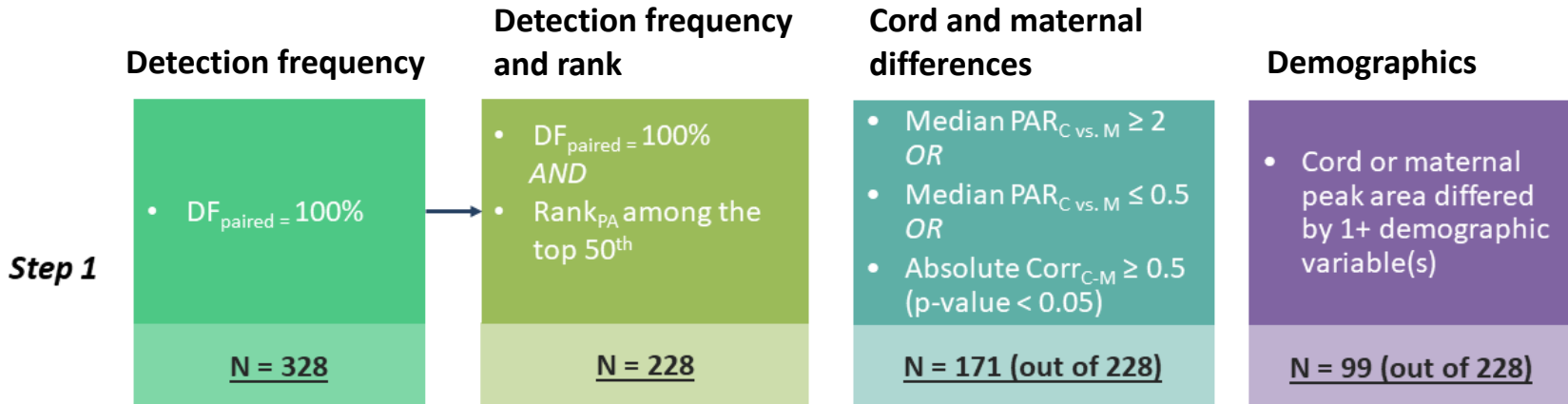
MS/MS in
ESI+/- for selected
features



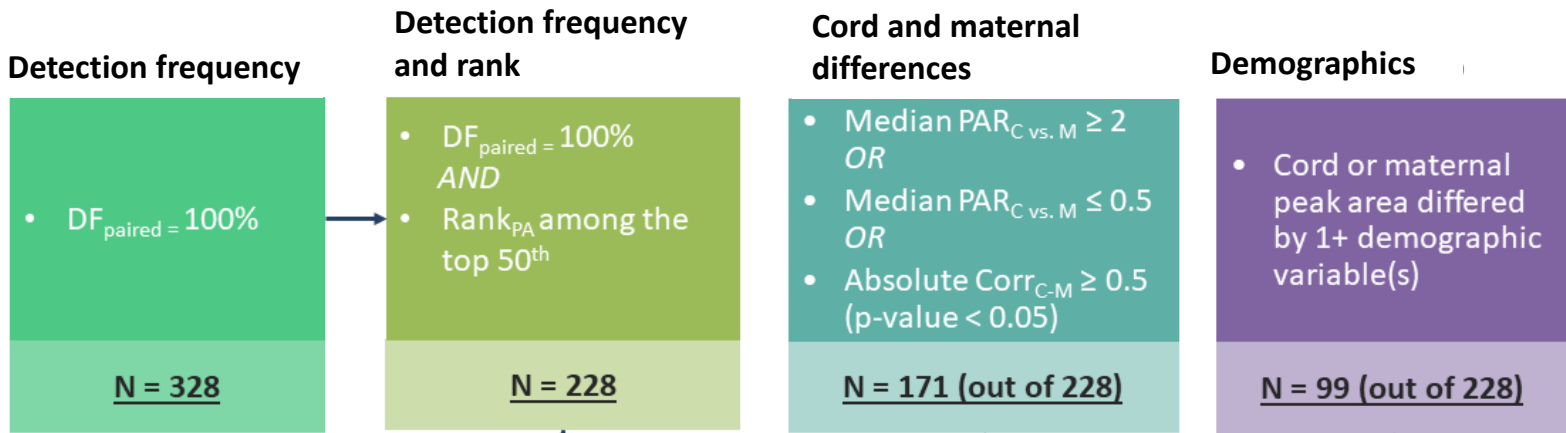
Confirmation with
analytical standards



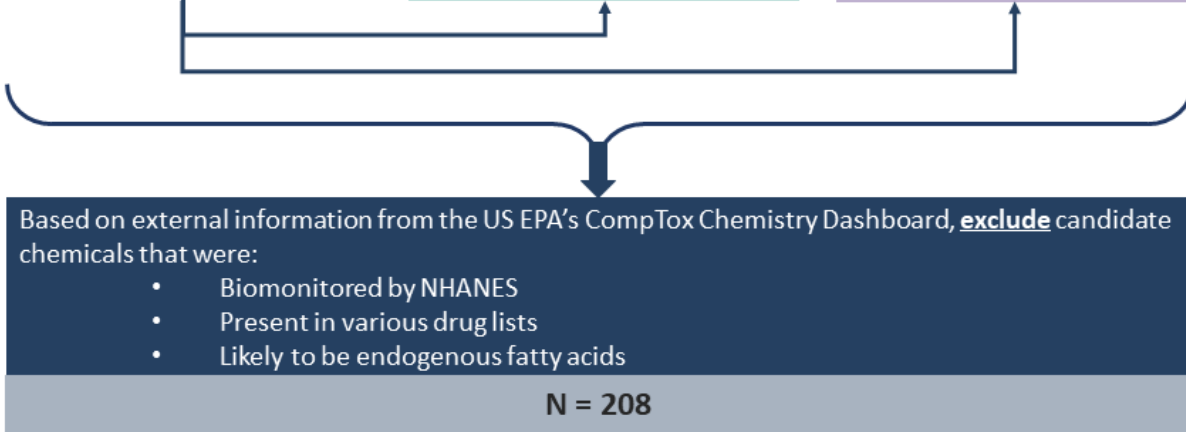
Only looking at features with 100% detection frequency

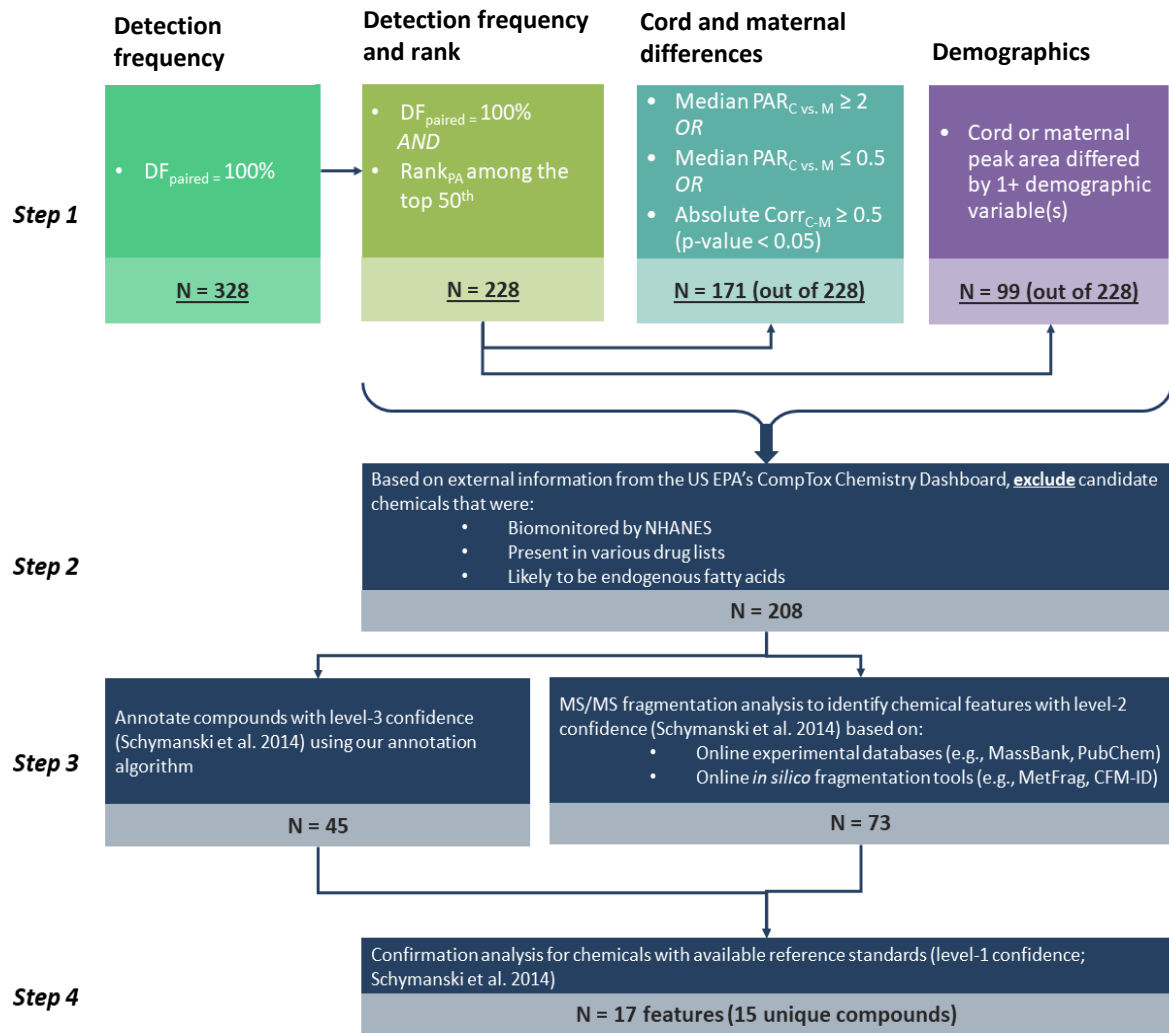


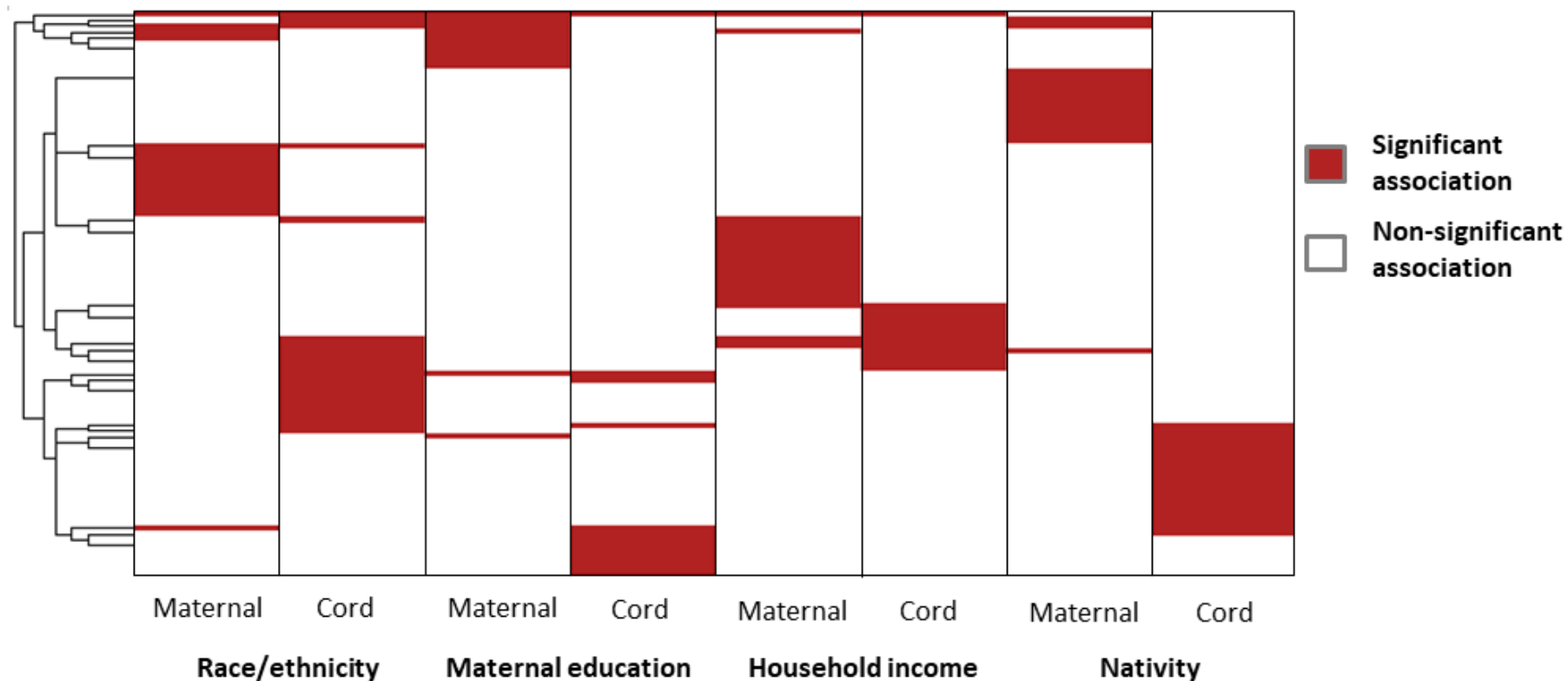
Step 1



Step 2





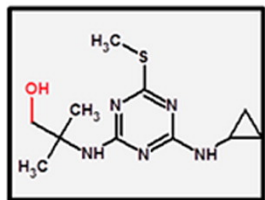


Communicating confidence in confirmation of compounds through HRMS

Example

Identification confidence

Minimum data requirements

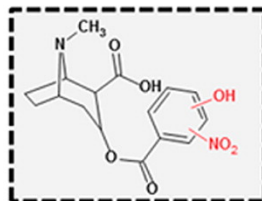


Level 1: Confirmed structure
by reference standard

MS, MS^2 , RT, Reference Std.

Level 2: Probable structure
a) by library spectrum match
b) by diagnostic evidence

MS, MS^2 , Library MS^2
MS, MS^2 , Exp. data



Level 3: Tentative candidate(s)
structure, substituent, class

MS, MS^2 , Exp. data

$\text{C}_6\text{H}_5\text{N}_3\text{O}_4$

Level 4: Unequivocal molecular formula

MS isotope/adduct

192.0757

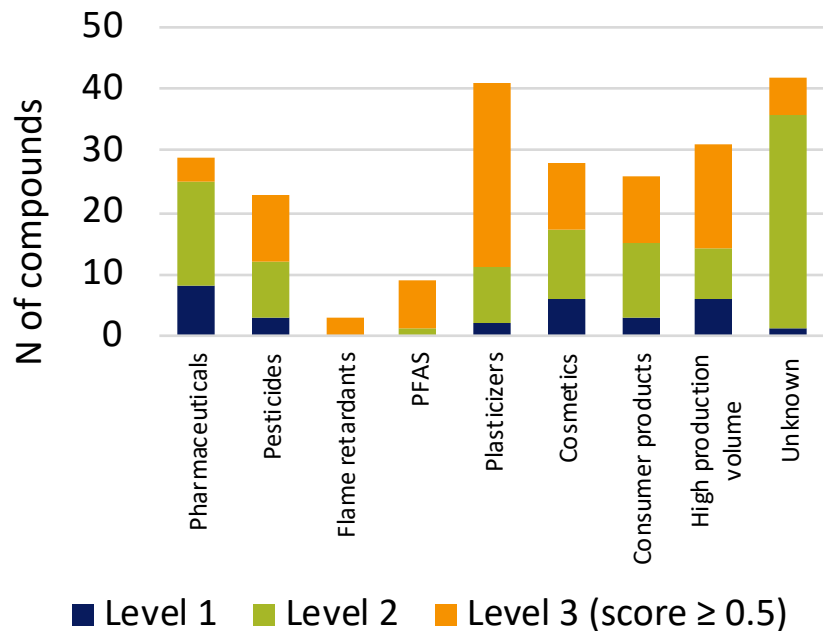
Level 5: Exact mass of interest

MS

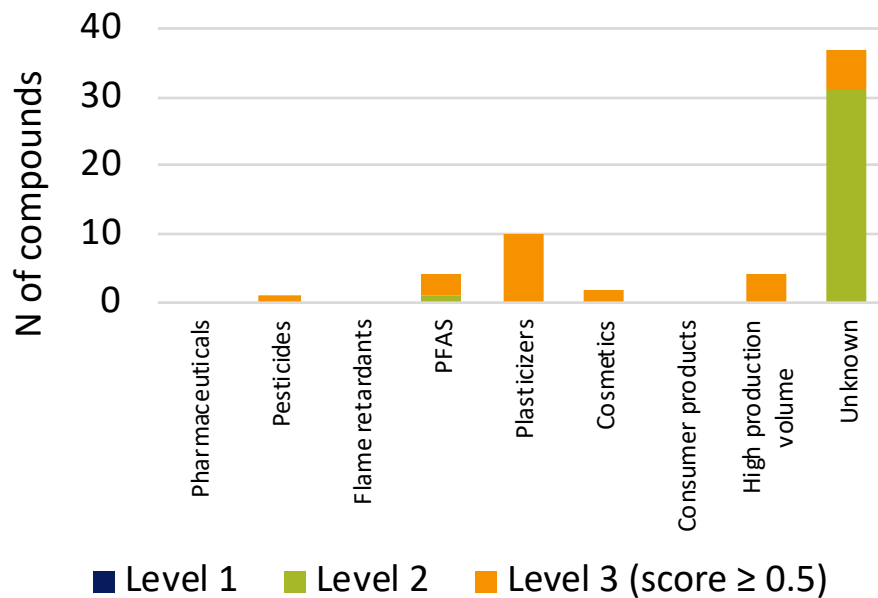


Sources and uses of chemicals in maternal and cord samples

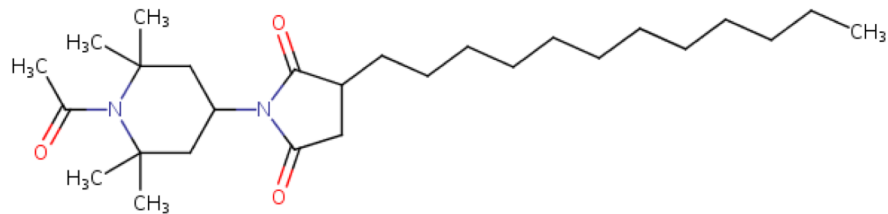
All compounds



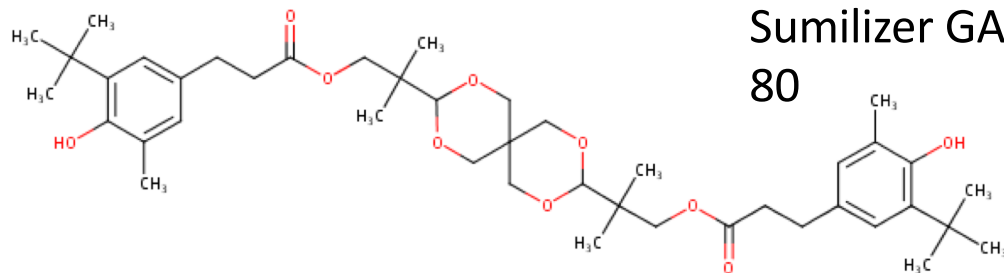
Not previously reported



1-(1-Acetyl-2,2,6,6-tetramethylpiperidin-4-yl)-3-dodecylpyrrolidine-2,5-dione

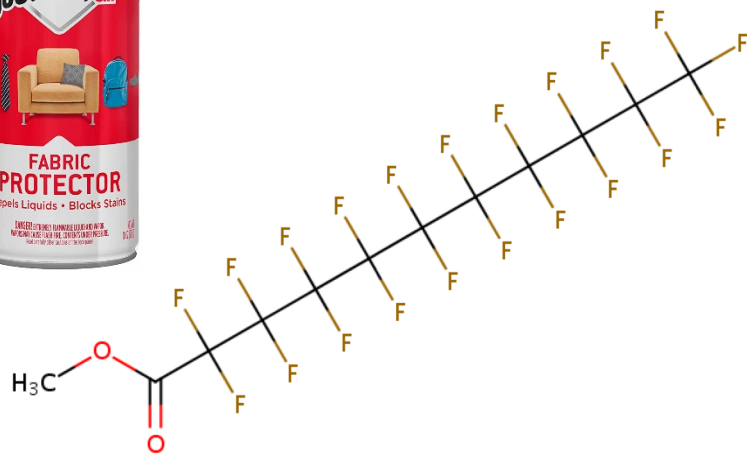


Consumer products, personal care, fragrances



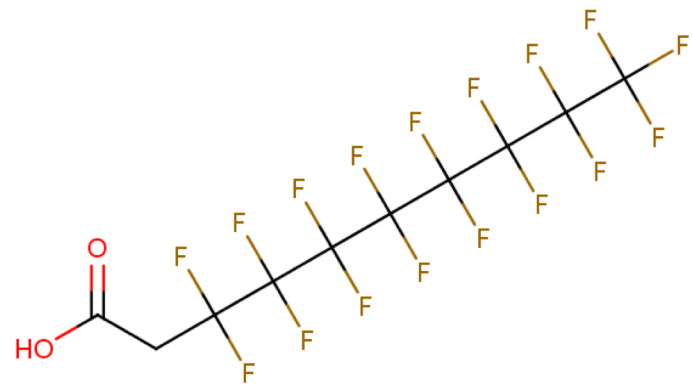
Plasticizer, used in the production of plastic polymers





methyl perfluoroundecanoate

Impurity of PFNA (used in fluoropolymer manufacture) and also a break down product of long-chain fluorotelomer-based products



2-perfluorooctyl ethanoic acid

Most probably derived from long-chain fluorotelomer products used as surface protectors in textiles, food contact materials, carpets, etc. (i.e. fluorotelomer-based side-chain fluorinated polymers that were typically acrylates)



Conclusions

- Non-targeted analysis / suspect screening methods are valuable tools in uncovering previously unknown exposures.
- These findings can then be used to inform biomonitoring studies and toxicity testing.
- There are numerous chemicals that we are exposed to but remain unknown
- Analytical standard availability is an important roadblock and prevents scientists from confirming many chemicals and quantifying their levels.
- The US EPA needs to request analytical standards from chemical manufacturers for all chemicals on the market.





Projects:
P01ES022841,
R01ES027051,
K01LM012381



@DimiAbrams
@TraceyJWoodruff
@UCSF_PRHE



Thank you!

<https://prhe.ucsf.edu/>

Program on Reproductive Health and the
Environment

UCSF

University of California
San Francisco





For more information
prhe.ucsf.edu

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