OPPT Briefing

Starter slides

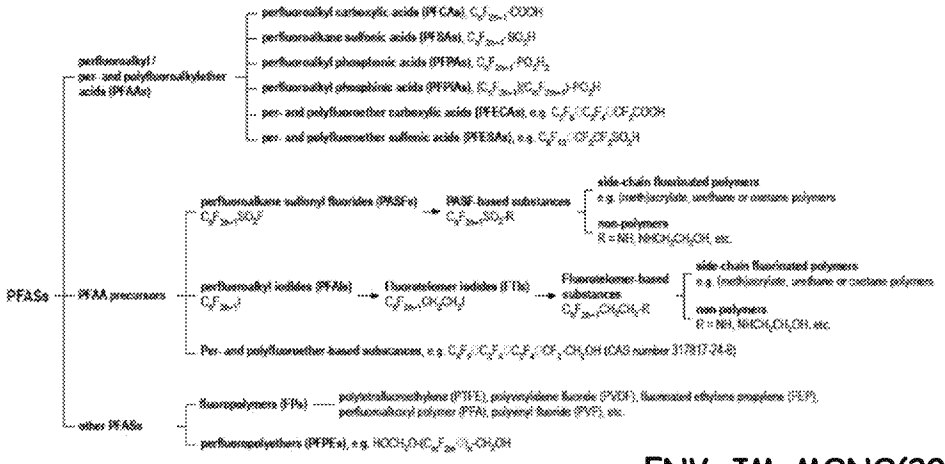
OECD Work

- Aimed to reconcile the terminology of the universe of per and polyfluoroalkyl substances, building largely on the terminology described by Buck et al (2011) but addressing some of the ambiguity and shortcomings of the original definition he proposed.
- OECD/UNEP Global PFC drafting group convened between June 2018-March 2021 to review the universe and terminology of PFAS
- "..fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon (without any H/Cl/Br/I atom attached to it).."
- Next slide shows a comprehensive overview of PFAS groups, structural traits and notes on whether corresponding common nomenclatures already exist

PFASs
perfluoroalkyl acids (PFAAs; including perfluoroalkylether acids, PFEAAs)
perfluoroalkyl carboxylic acids (PFCAs), C_nF_{2n+1}-COOH
perfluoroalkane sulfonic acids (PFSAs), C_nF_{2n+1}-SO_3H
perfluoroalkyl phosphonic acids (PFPAs), C_nF_{2n+1}-PO_3H_2
perfluoroalkyl phosphinic acids (PFPIAs), $(C_nF_{2n+1})(C_mF_{2m+1})$-$PO_2H$
perfluoroalkylether carboxylic acids (PFECAs), e.g. C_2F_5◇C_2F_4◇CF_2COOH
perfluoroalkylether sulfonic acids (PFESAs), e.g. C_6F_{13}◇$CF_2CF_2SO_3H$
perfluoroalkyl dicarboxylic acids (PFdICAs), HOOC-C_nF_{2n}-COOH
perfluoroalkane disulfonic acids (PFdISAs), HO_3S-C_nF_{2n}-SO_3H
perfluoroalkane sulfinic acids (PFSIAs), C_nF_{2n+1}-SO_2H
polyfluoroalkyl acids (PolyFAAs; including polyfluoroalkylether acids, PolyFEAAs)*
polyfluoroalkyl carboxylic acids (PFCAs or PolyFCAs), e.g. H-C_nF_{2n}-COOH, n>2
polyfluoroalkylether carboxylic acids (PFECAs), e.g. CF_3◇C_3F_6◇C◇FCF_2COOH
polyfluoroalkylether sulfonic acids (PFESAs), e.g. ◇C_6F_{12}◇$CF_2CF_2SO_3H$
PFAA precursors
n:1 fluorotelomer alcohols, $C_nF_{2n+1}CH_2OH$
n:1 fluorotelomer-based substances, $C_nF_{2n+1}CH_2$-R
perfluoroalkanoyl fluorides (PACFs), C_nF_{2n+1}COF
PACF-based substances, $C_nF_{2n+1}CO_2$-R
perfluoroalkyl iodides (PFAIs), $C_nF_{2n+1}I$
n:2 fluorotelomer-based substances, $C_nF_{2n+1}CH_2CH_2$-R
perfluoroalkane sulfonyl fluorides (PASFs), $C_nF_{2n+1}SO_2F$
PASF-based substances, $C_nF_{2n+1}SO_2$-R
side-chain fluorinated polymers e.g. (meth)acrylate, methylene or methane polymers, silicones
non-polymers
R = NH, $NHCH_2CH_2OH$, etc.
perfluoroalkylether non-polymers, e.g. C_4F_9◇C_2F_4◇C_2F_4◇CF_2-CH_2OH, CAS No. 317817-24-6
perfluoroalkylether side-chain fluorinated polymers
perfluoroalkenes (C_nF_{2n}, n>2)
perfluoroalkene derivatives, e.g. $[(CF_3)_2CF]_2C$=$C(CF_3)OC_6H_4SO_3Na$), CAS No. 70829-87-7
semifluorinated alkanes (SFAs), C_nF_{2n+1}-C_mH_{2m+1}
hydrofluorocarbons (HFCs, e.g. C_nF_{2n+1}-C_mH_{2m+1}), hydrofluoroethers (HFEs, e.g. C_nF_{2n+1}◇C_mH_{2m+1}), hydrofluoroolefins (HFOs, e.g. C_nF_{2n+1}-CH=CH_2) that have a perfluoroalkyl chain
perfluoroalkyl (e.g. $C_nF_{2n+1}C(O)C_mF_{2m+1}$) and semi-fluorinated ketones (e.g. $C_nF_{2n+1}C(O)C_mH_{2m+1}$)
perfluoroalkyl alcohols ($C_nF_{2n+1}OH$), e.g. $(CF_3)_3C$-OH, CAS No. 2378-02-1
other PFASs
fluoropolymers (FPs)
polytetrafluoroethylene (PTFE)
polyvinylidene fluoride (PVDF)
fluorinated ethylene propylene (FEP)
perfluoroalkoxyl polymer (PFA)
Other FPs
perfluoropolyethers (PFPEs), e.g. $HOCH_2O$-$(C_nF_{2n}O)_x$-CH_2OH
side-chain fluorinated aromatics**, e.g. C_nF_{2n+1}-aromatic rings
perfluoroalkanes (C_nF_{2n+2})
perfluoroalkyl-*tert*-amines $(C_nF_{2n+1})_3N$
perfluoroalkylethers (e.g. $C_nF_{2n+1}OC_mF_{2m+1}$)
others***
Nomenclature including acronyms well covered by Buck et al. (2011)
Nomenclature including acronyms partially covered by Buck et al. (2011)
Common nomenclature including acronyms exists
Indicating that it is a synthesis pathway, instead of examples
Polymeric PFASs
Note: This figure is intended to be comprehensive, but not exhaustive; in other words, there are other groups of PFASs that are not captured in this figure.
* It is recommended that *poly*fluoroalkyl acids use the acronym *Poly*FAA to better distinguish from *per*fluoroalkyl acids. Depending on the fluorination degree and location, *poly*fluoroalkyl carboxylic acids may either be highly persistent themselves, or act as precursors to other PFAAs such as PFdICAs, under natural conditions.
** Depending on the type of linkages between fluorinated side chain(s) and aromatic ring(s), some side-chain fluorinated aromatics may act as precursors to PFAAs or PFEAAs.
*** Depending on the molecule structure, one may belong to PFAAs, PolyFAAs, PFAA precursors, or other groups that are not described here.

Existing OECD terminology

a) Commonly recognized per- and polyfluoroalkyl substances (PFASs)



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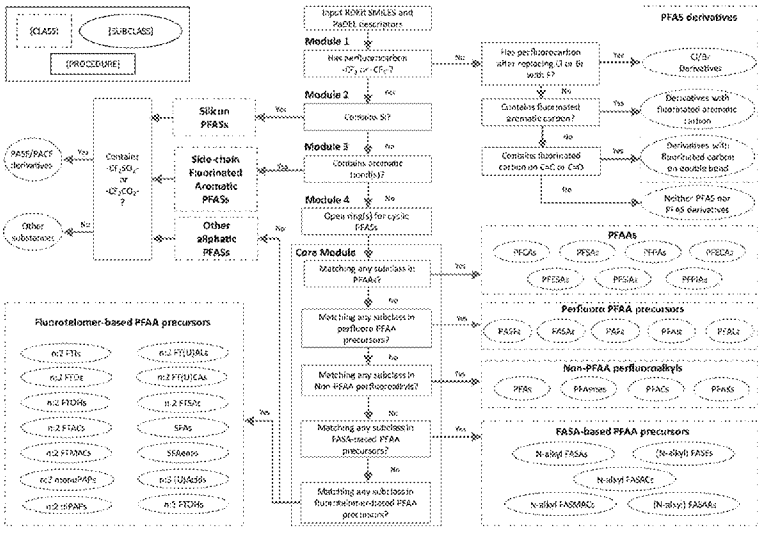
PFAS Map

- Su, A., Rajan, K. A database framework for rapid screening of structure-function relationships in PFAS chemistry. Sci Data 8, 14 (2021). https://doi.org/10.1038/s41597-021-00798-x



PFAS Map

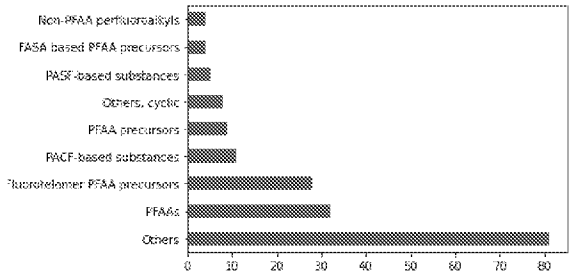
- Nine broad categories are captured:
  - PFAS derivatives
  - PFAAs
  - Perfluoro PFAA precursors
  - Non-PFASS perfluoroalkyls
  - FASA-based PFASS precursors
  - Fluorotelomer-based PFAA precursors
  - Silicon PFASs
  - Side-chain fluorinated Aromatics PFASs
  - Other aliphatic PFASs

Mapping to TxP structural categories

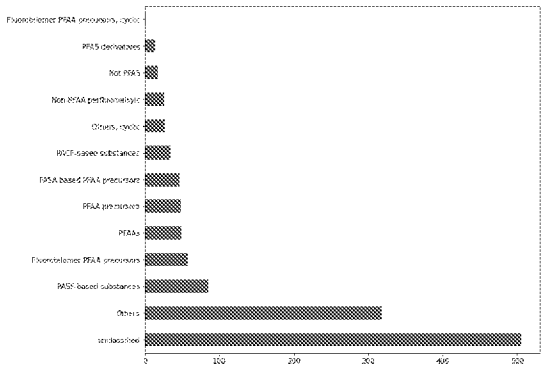
- Richard and colleagues devised a set of 34 structural categories (TxP Categories) which rely on publicly accessible ToxPrint fingerprints (part of the 729 ToxPrint chemotypes published by Yang et al (2015) which are a fixed set of chemical features characterised by atom, bond and functional group representations)
- TxP categories can be assigned systematically using chemical structure.
- TxP categories are mainly bounded by their functional group e.g. TxP_PFAS_alcohol, TxP_PFAS_COOH_FT
- One or more TxP category can be assigned to a substance i.e. many to one mapping
- Moreover, each TxP category can be mapped to one or more PFAS Map category i.e. TxP categories are helpful in subcategorising within these OECD Broader categories as implemented within the PFAS Map resource.

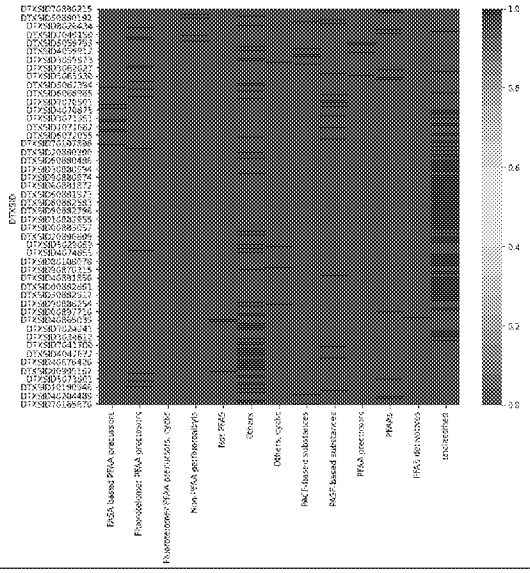
PFAS Map

- Used PFAS Map to profile PFAS into one of the broad categories
- Illustrative profiling for the PFAS being tested in the suite of NAM assays



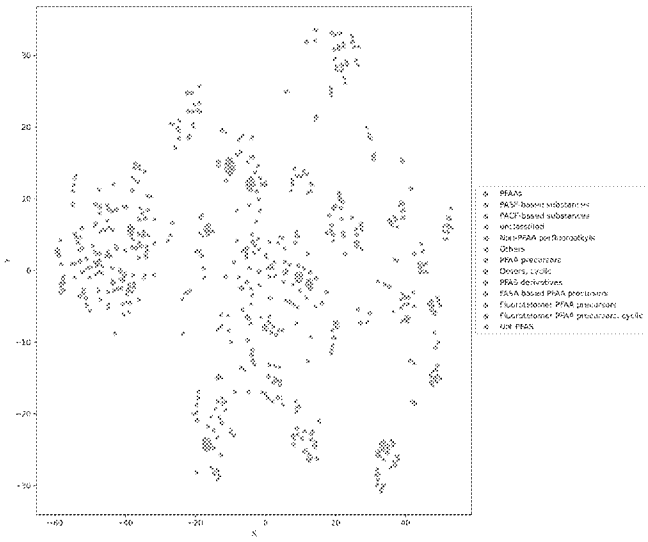
PFAS Map on 'Union of Lists'



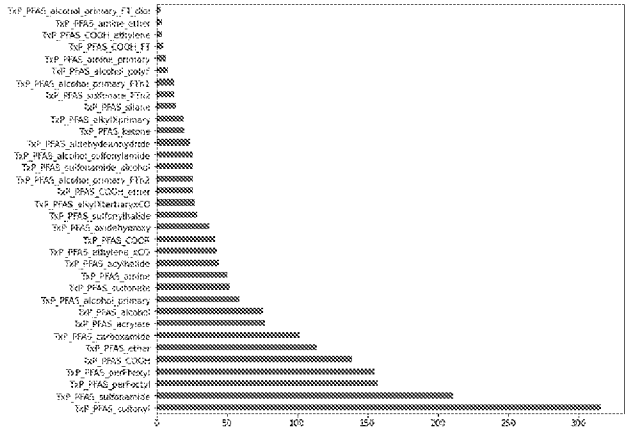


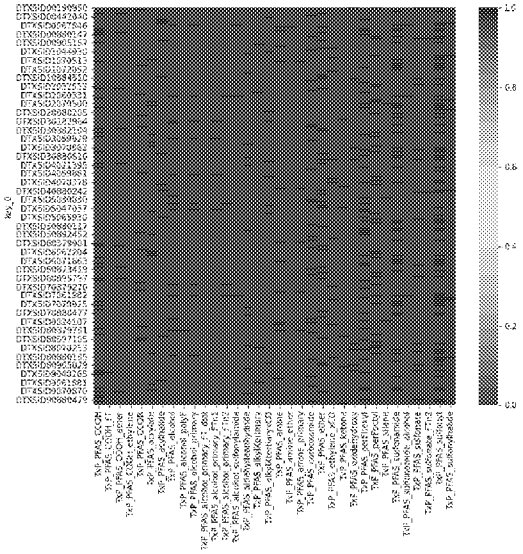
TSNE mapping of Union of Lists

TxP fingerprints for structurable substances – mapped to the PFAS Map categories

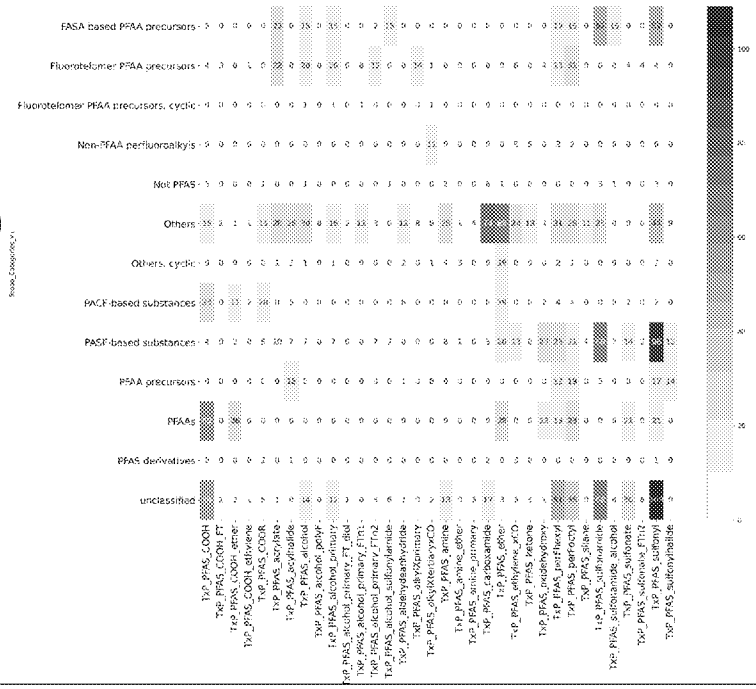


TxP categories profiling on Union of Lists

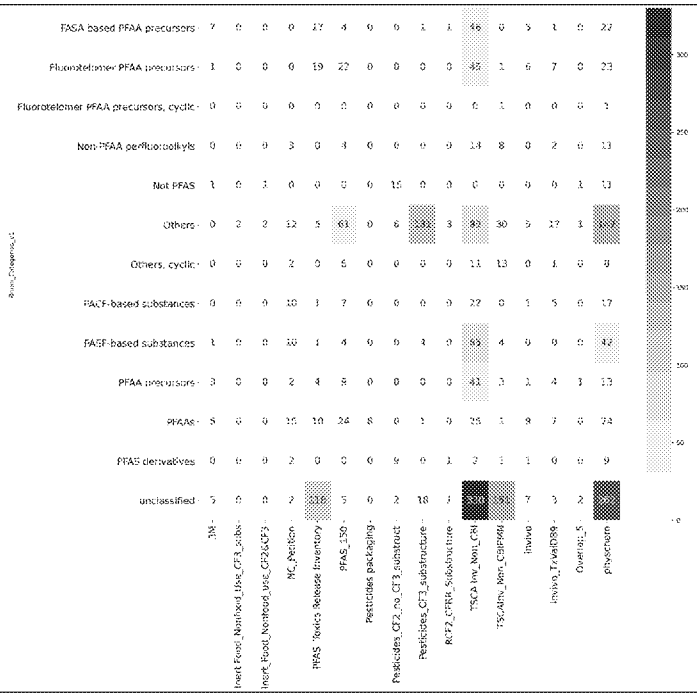




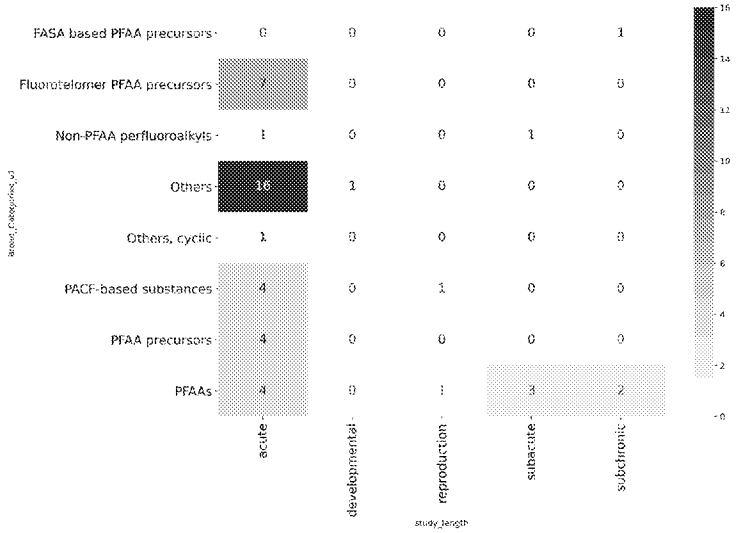
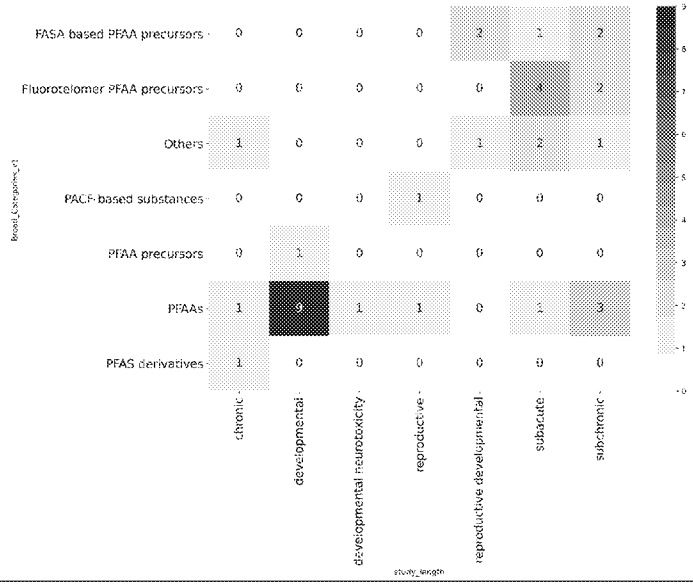
PFAS Map vs TxP counts



Categories vs Union List of lists & toxicity data



In vivo (ToxValDB v9) data by category



In vivo (curated) data by category