The background of the slide is a soft, teal-colored landscape. It features a calm body of water in the foreground, reflecting the sky. In the distance, there are rolling hills or mountains, some of which are shrouded in a light mist or fog. The overall atmosphere is serene and somewhat ethereal.

To Be Or Not To Be a PFAS: That is the Question.

There are more PFAS in heaven and earth, Horatio, than are dreamt of in your definition

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U.S. EPA, Office of Superfund Remediation and Technology Innovation

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Note

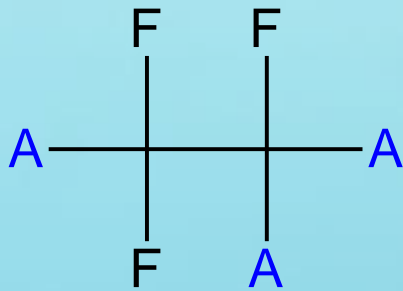
- Numerous chemical structures are included in this presentation to provide examples of how the different definitions of PFAS differ. The structures were found in EPA's CompTox Chemicals Dashboard (<https://comptox.epa.gov/dashboard/>). Importantly, the presence of a chemical in the Dashboard does not mean the chemical is present in the environment or has ever been manufactured or created.

How PFAS have been defined

- One $\text{-CF}_2\text{-}$ group in the molecular structure
 - Over 38,000 structures in EPA's CompTox Chemicals Dashboard (Dashboard)
 - Definition used by Organisation for Economic Cooperation and Development (OECD) in 2021
 - OECD specifies a fully fluorinated C, which is slightly different definition
 - Definition used by Congress in many bills since (at least) 2020
- ONLY aliphatic structures with one $\text{-CF}_2\text{-}$ group
 - Over 13,000 structures in the Dashboard
 - Definition used in the text of Buck et al. 2011
- ONLY aliphatic structures with one $\text{CF}_3\text{-}$ group
 - Over 10,000 structures in the Dashboard
 - Definition used in the moiety described of Buck et al. 2011 (the text and the moiety do not match)

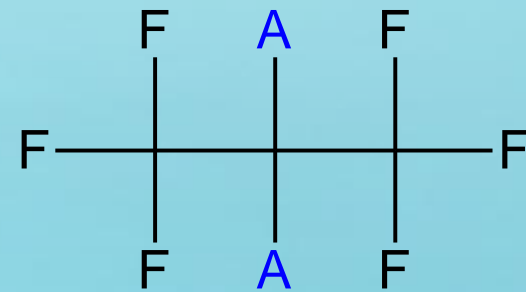
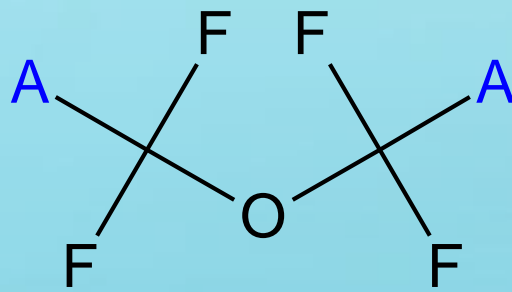
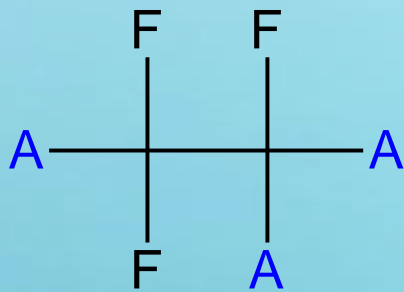
How PFAS have been defined by EPA

- $R-(CF_2)-C(F)(R')R''$, both C saturated, no R groups are H
 - Over 9,000 structures in the Dashboard
 - Definition used by OCSPP in 2021 for proposed TSCA Section 8(a)(7) reporting rule EPA-HQ-OPPT-2020-0549; FRL-10017-78
 - Definition used by OW in 2021 for draft Contaminant Candidate List (CCL5) rule EPA-HQ-OW-2018-0594; FRL-7251-01-OW



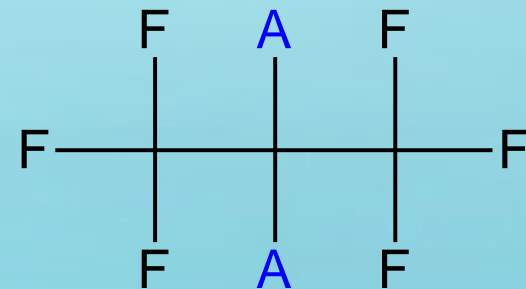
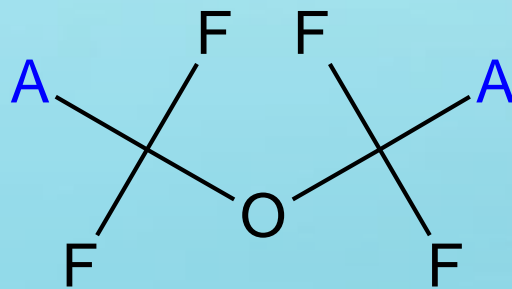
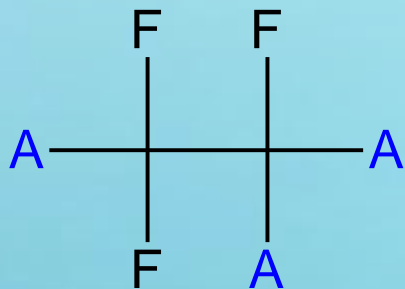
How PFAS have been defined by EPA

- Three substructures
 - Over 10,000 structures in Dashboard
 - $R-(CF_2)-CF(R')R''$, where both the CF_2 and CF moieties are saturated carbons, and none of the R groups can be H
 - $R-CF_2O-CF_2-R'$, where both the CF_2 moieties are saturated carbons, and none of the R groups can be H
 - $CF_3C(CF_3)RR'$, where all the carbons are saturated, and none of the R groups can be H
 - Definition used by OW in 2022 for final CCL5 rule EPA-HQ-OW-2018-0594; FRL-7251-01-OW



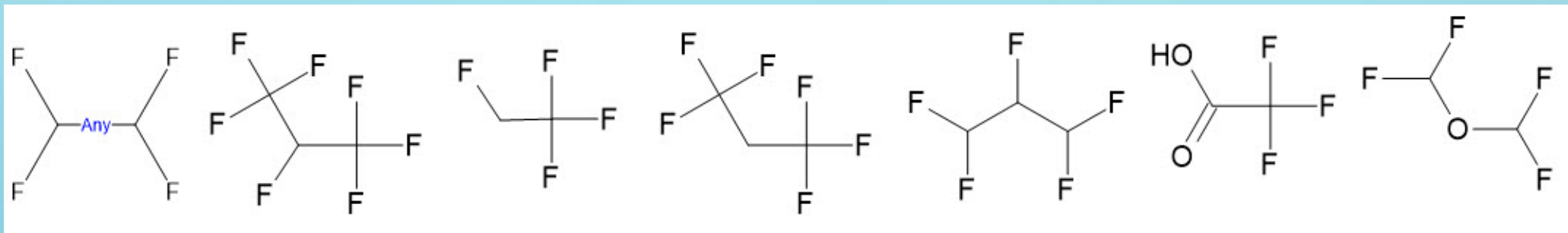
How PFAS have been defined by EPA

- Three substructures
 - Over 11,000 structures in Dashboard
 - $R-(CF_2)-CF(R')R''$, where both the CF_2 and CF moieties are saturated carbons
 - $R-CF_2O-CF_2-R'$, where R and R' can either be F , O , or saturated carbons
 - $CF_3C(CF_3)RR'$, where R' and R'' can either be F or saturated carbons
 - Definition used by OCSPP in 2023 for final updated TSCA 8(a)(7) rule EPA-HQ-OPPT-2020-0549; FRL-7902-02-OCSPP



How PFAS have been defined by EPA

- At least one of the substructures below
 - Over 11,000 structures in the Dashboard
 - Definition used for the Dashboard PFAS structures list version 3 and 4
 - If trifluoroacetic acid (TFA, 6th from left) is removed, 500 structures removed

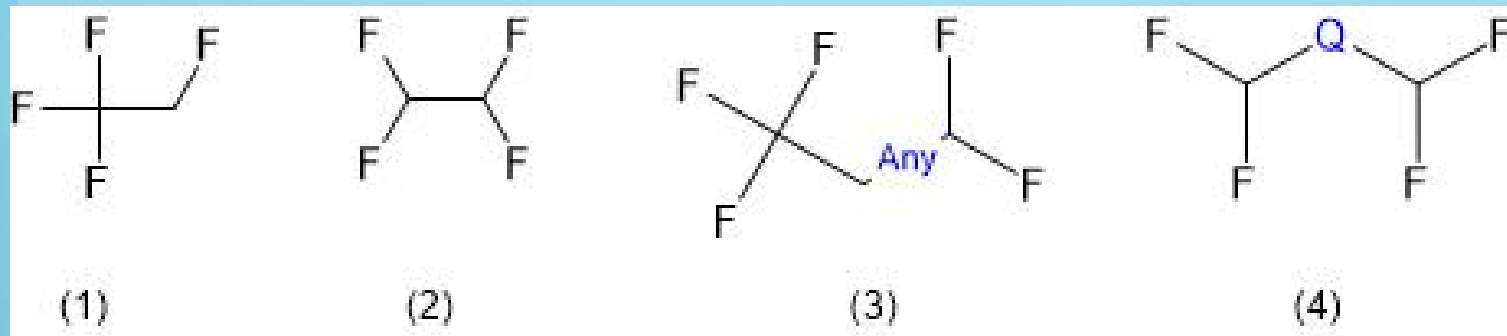


Refining Dashboard PFAS structures list

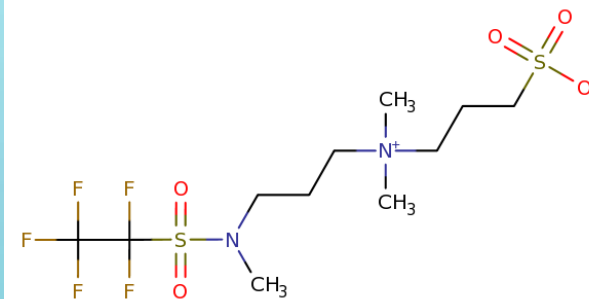
- In comparing various PFAS definitions, Dashboard PFAS structures list needed additional substructures
 - Structures were on TSCA 2021 list not on Dashboard list
 - Some highly branched or otherwise complex structures also not captured
- Compared structures on TSCA or OECD lists but not Dashboard list to see what substructures needed
- Limited comparison to not include structures
 - Less than 3 F
 - Only 1 terminal CF₃
- Determined at least 15 substructures needed to capture all PFAS

New Definition (PFASSTRUCTv5)

- 30% F based on fraction of molecular formula excluding H
 - For example, for $C_6HF_9O_6$, the F percent excluding H contained in the formula would be $9F / (6C + 9F + 6O) = 42\%$
 - OECD (2021) argued against using a weight percent F, but this is simply a count percent and excludes atomic weight
- Or contains one of four substructures
 - For substructure 4, Q can be B, O, N, P, S, or Si
- Over 14,500 structures in Dashboard



DTXSID901035057 (20%F)
with PFES substructure



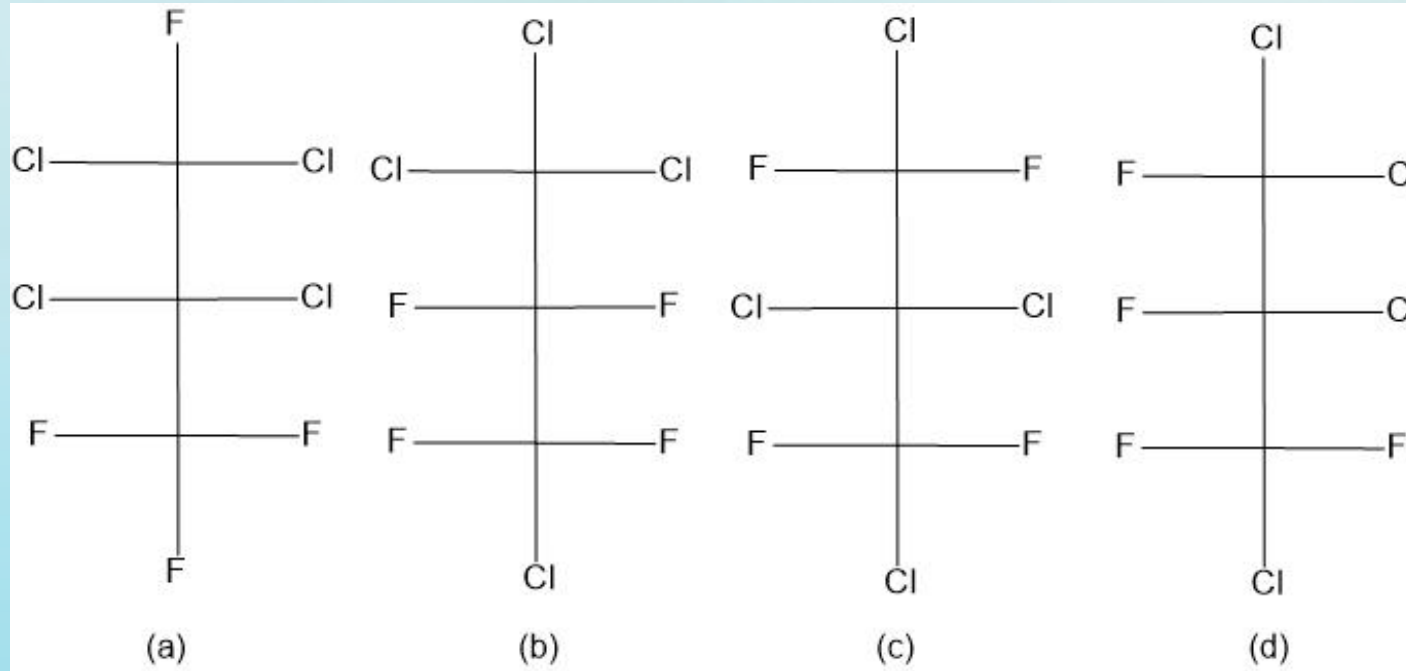


Poll Question

Definition complications

- Aliphatic versus aromatic
- Branching
- Ethers (-O-)
- Other halogens (Cl, Br, and I)
- Hydrogen
- Double and triple bonds
- Combination of all of the above

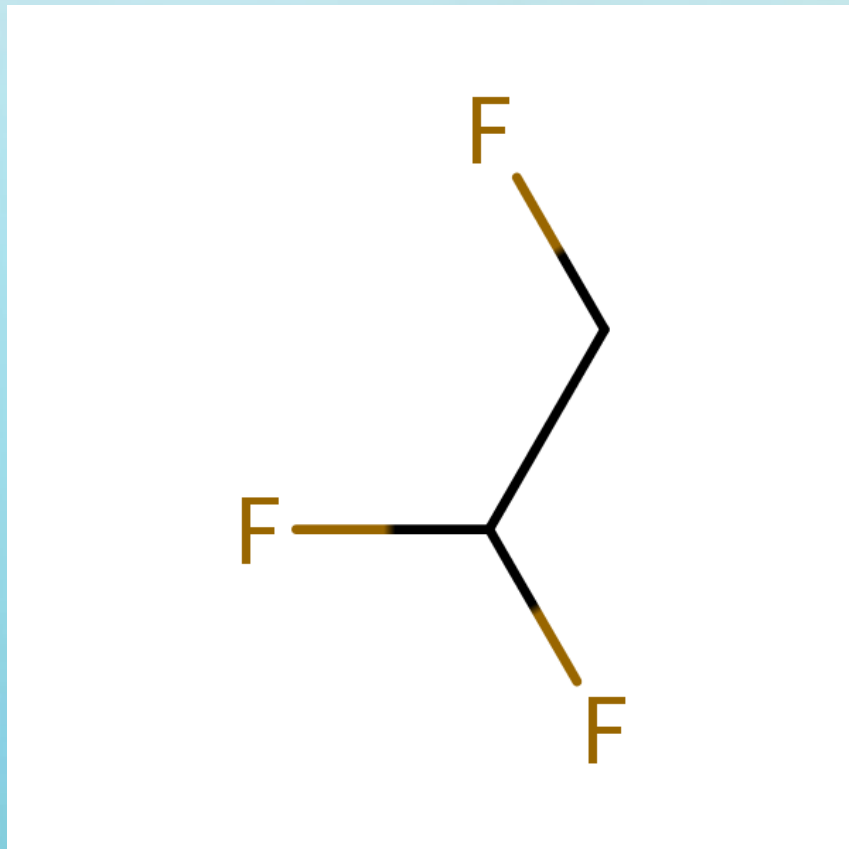
Maybe, Maybe Not PFAS - Isomers



A	B	C	D
OECD - Y	OECD - Y	OECD - N	OECD - N
OW/OCSPP 2021 - N	OW/OCSPP 2021 - Y	OW/OCSPP 2021 - N	OW/OCSPP 2021 - Y
PFASSTRUCTv5 - Y	PFASSTRUCTv5 - Y	PFASSTRUCTv5 - Y	PFASSTRUCTv5 - Y
OW 2022 - N	OW 2022 - Y	OW 2022 - N	OW 2022 - Y
OCSPP 2023 - N	OCSPP 2023 - Y	OCSPP 2023 - N	OCSPP 2023 - Y

Maybe, Maybe Not PFAS – Terminal C

1,1,2-Trifluoroethane

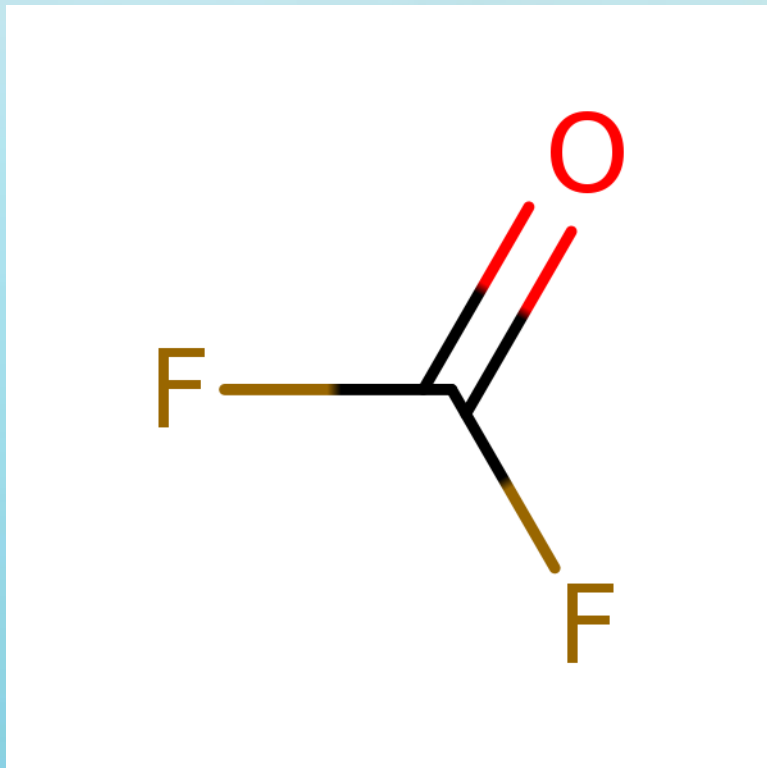


PFAS?

Definition	PFAS?
OECD	No
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	No
OCSP 2023	Yes

Maybe, Maybe Not PFAS – Terminal C

Carbonyl difluoride
(Fluorophosgene)

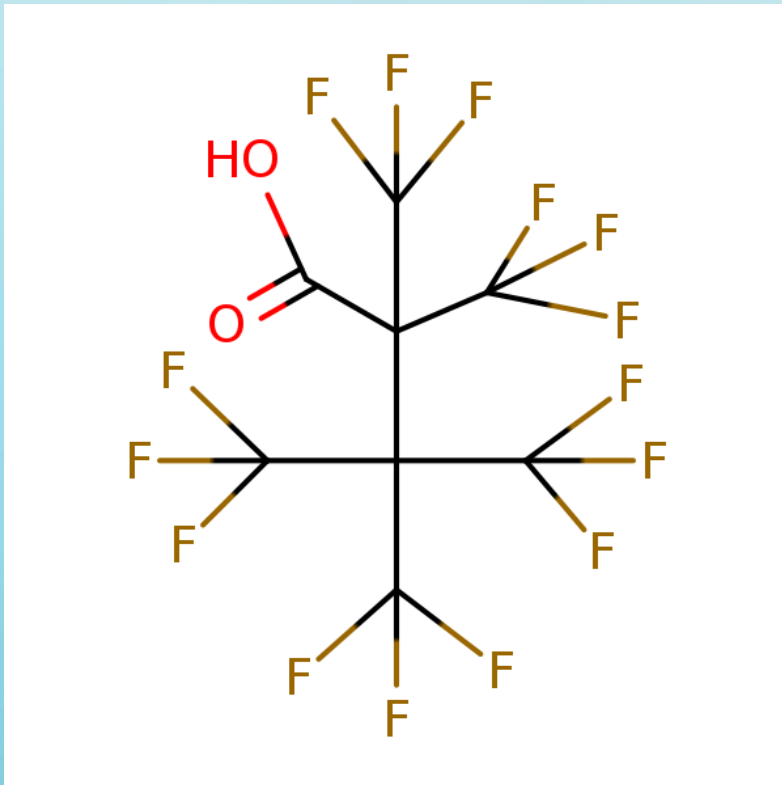


PFAS?

Definition	PFAS?
OECD	No
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	No
OCSP 2023	No

Maybe, Maybe Not PFAS – Branching

Perfluoro-2,2,3,3-tetramethylbutanoic acid (PFOA)

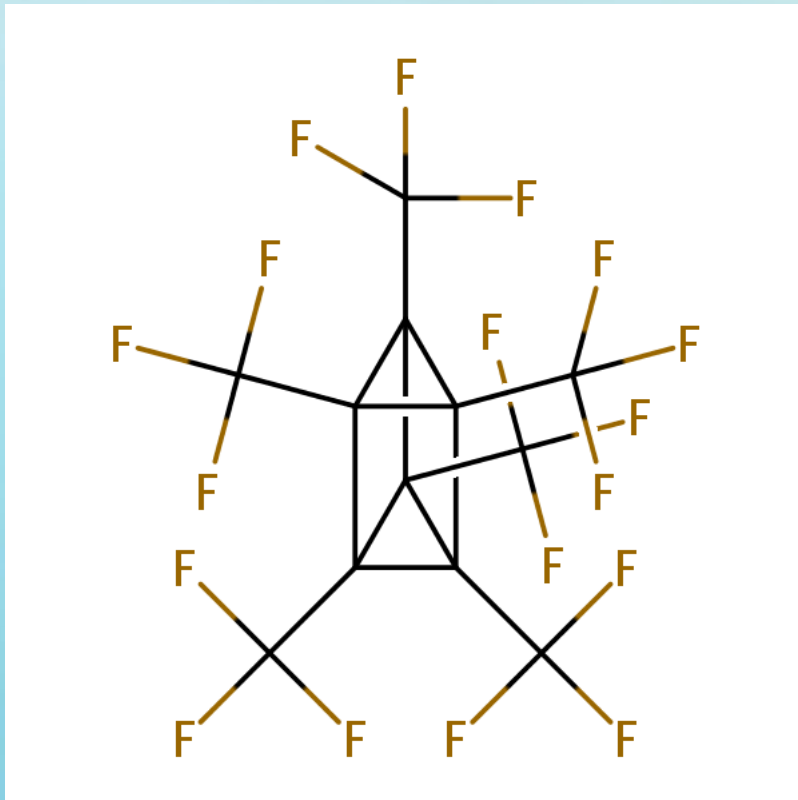


PFAS?

Definition	PFAS?
OECD	Yes
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	Yes
OCSP 2023	Yes

Maybe, Maybe Not PFAS – Branching

Perfluorohexamethylprismane

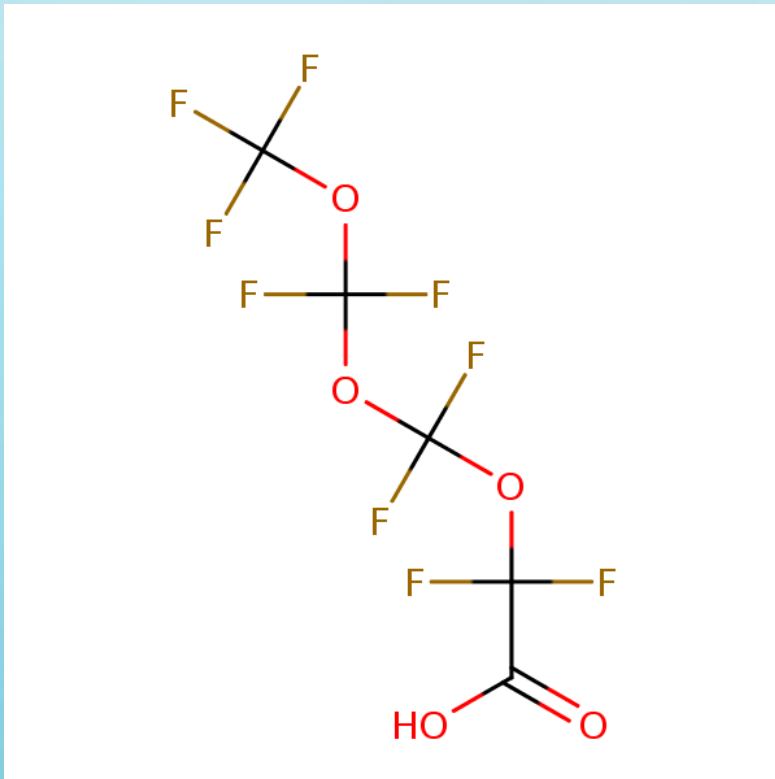


PFAS?

Definition	PFAS?
OECD	Yes
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	No
OCSP 2023	No

Maybe, Maybe Not PFAS – Ethers

Perfluoro-3,5,7-trioxaoctanoic acid

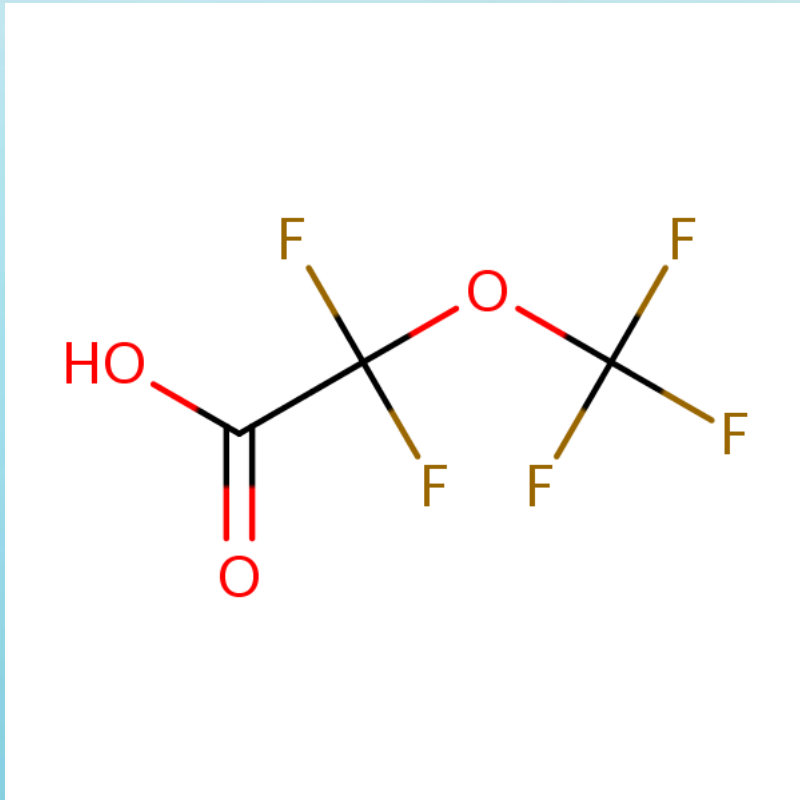


PFAS?

Definition	PFAS?
OECD	Yes
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	Yes
OCSP 2023	Yes

Maybe, Maybe Not PFAS – Ethers

Perfluoro-2-methoxyacetic acid

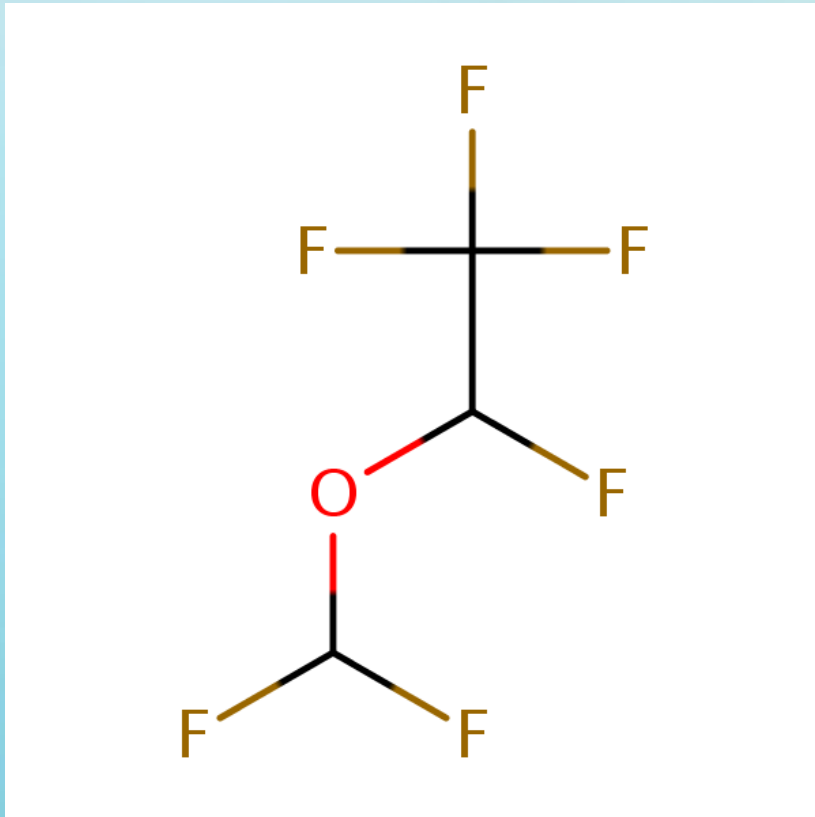


PFAS?

Definition	PFAS?
OECD	Yes
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	Yes
OCSP 2023	No

Maybe, Maybe Not PFAS – Ethers

Desflurane



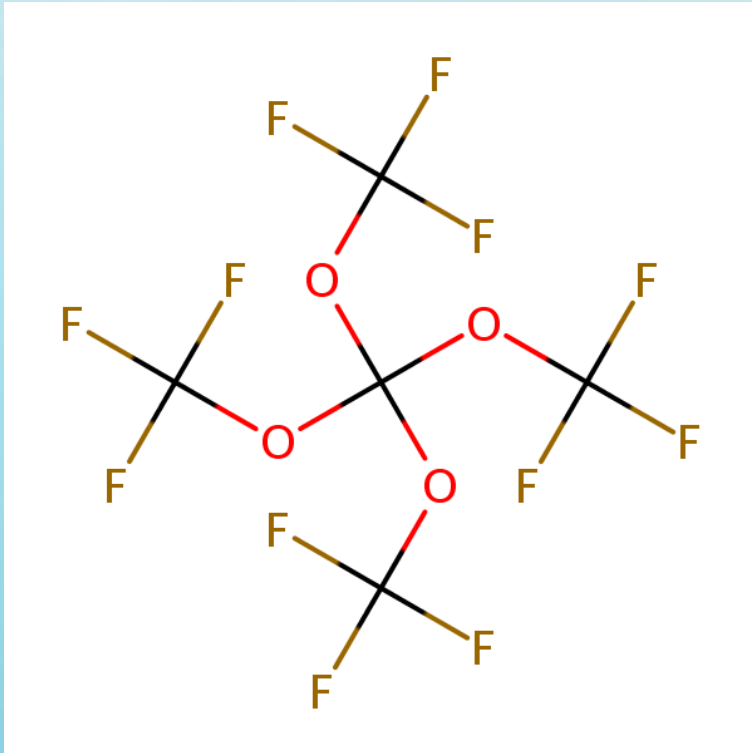
PFAS?

Definition	PFAS?
OECD	Yes
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	No
OCSP 2023	Yes

FDA approved drug for maintenance of general anesthesia

Maybe, Maybe Not PFAS – Ethers

Tetrakis(trifluoromethoxy)methane

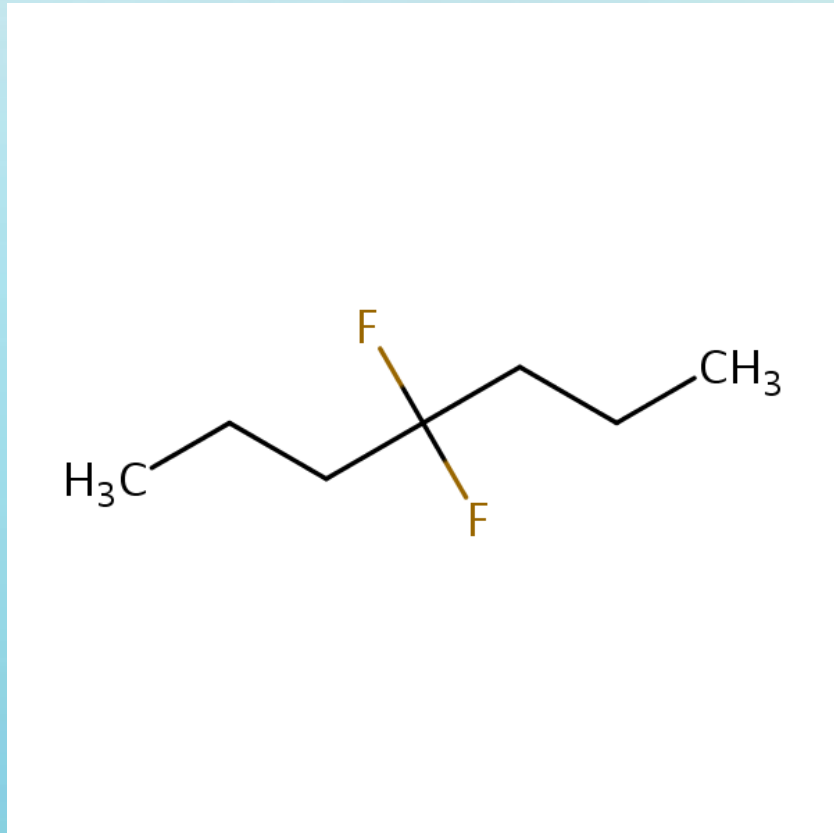


PFAS?

Definition	PFAS?
OECD	Yes
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	No
OCSP 2023	No

Maybe, Maybe Not PFAS – One CF₂

4,4-Difluoroheptane

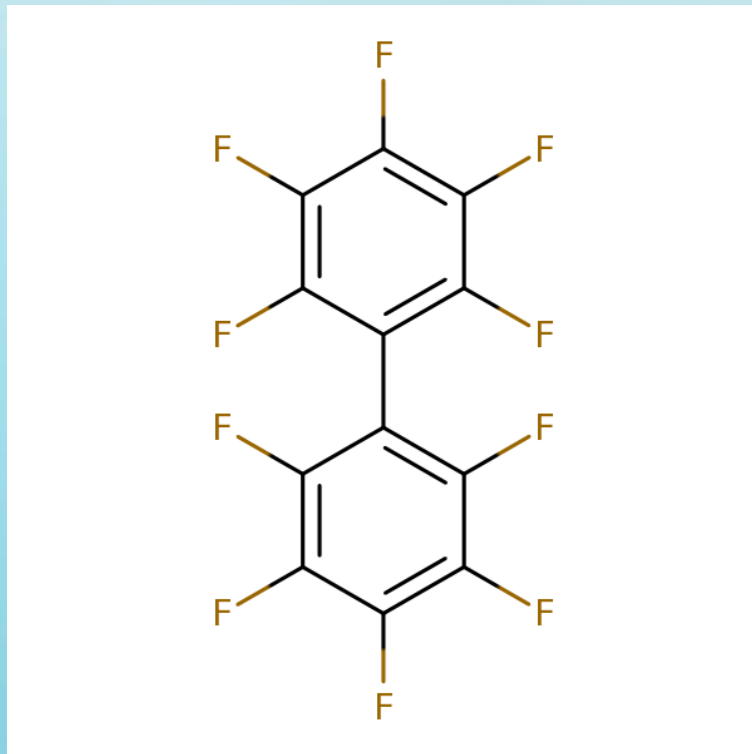


PFAS?

Definition	PFAS?
OECD	Yes
OW/OCSP 2021	No
PFASSTRUCTv5	No
OW 2022	No
OCSP 2023	No

Maybe, Maybe Not PFAS – Aromatic

Perfluorobiphenyl



PFAS?

Definition	PFAS?
OECD	No
OW/OCSP 2021	No
PFASSTRUCTv5	Yes
OW 2022	No
OCSP 2023	No

Conclusions

- No currently used definition is “most inclusive.”
- When creating a new definition, important to do in depth of analysis of what will and will not be included
- When using any definition, important to be clear on why that definition should be used. Also, be clear on which definition is being used.

For More Information

- Comparison of definitions in Williams et al. 2022 “Assembly and Curation of Lists of Per- and Polyfluoroalkyl Substances (PFAS) to Support Environmental Science Research” doi: 10.3389/fenvs.2022.850019
- New definition in Gaines et al. 2023 “A proposed approach to defining per- and polyfluoroalkyl substances (PFAS) based on molecular structure and formula” DOI: 10.1002/ieam.4735
- New definition results available at:
<https://comptox.epa.gov/dashboard/chemical-lists/PFASSTRUCTV5>
- Big thank you to my collaborator Antony Williams
- Contact: gaines.linda@epa.gov