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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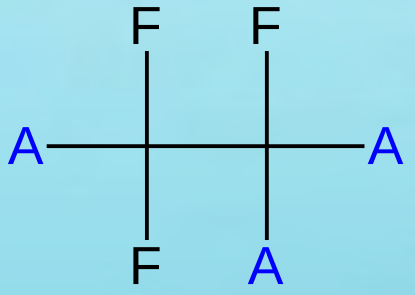
How PFAS have been defined

- One -CF_2- 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 -CF_2- group
  - Over 13,000 structures in the Dashboard
  - Definition used in the text of Buck et al. 2011
- ONLY aliphatic structures with one CF_3- 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)

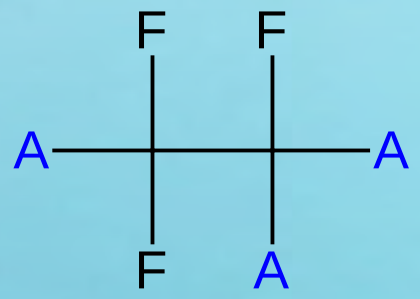
How PFAS have been defined by EPA

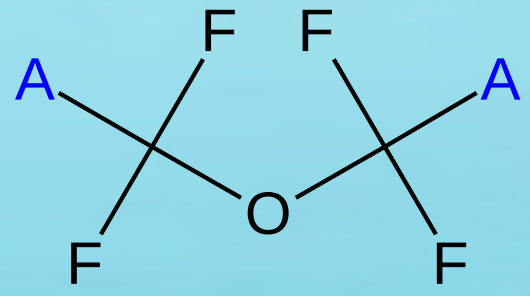
- R-(CF_2)-C(F)(R′)R″, both C saturated, no R groups are H
  - Over 9,000 structures in the Dashboard
  - Definition used by OCSPP in 2021 for proposed TSCA Section 8(a)(7) reporting rule EPA–HQ–OPPT–2020–0549; FRL–10017–78
  - Definition used by OW in 2021 for draft Contaminant Candidate List (CCL5)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

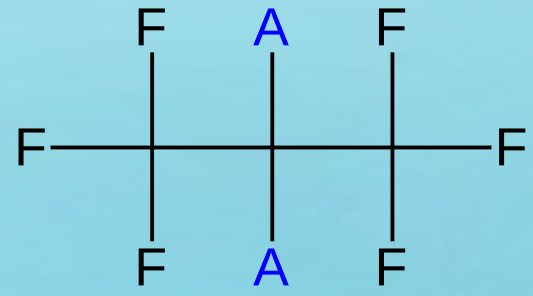


How PFAS have been defined by EPA

- Three substructures
  - Over 10,000 structures in Dashboard
  - R-(CF2)-CF(R')R", where both the CF2 and CF moieties are saturated carbons, and none of the R groups can be H
  - R-CF20CF2-R', where both the CF2 moieties are saturated carbons, and none of the R groups can be H
  - CF3C(CF3)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

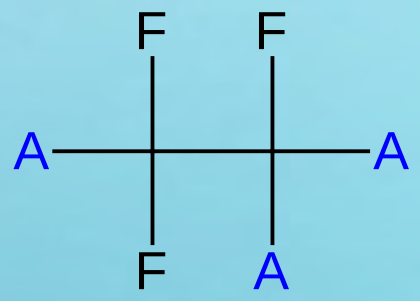


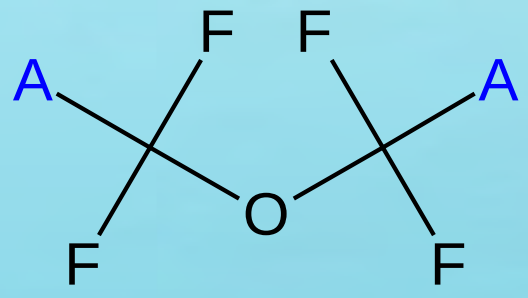


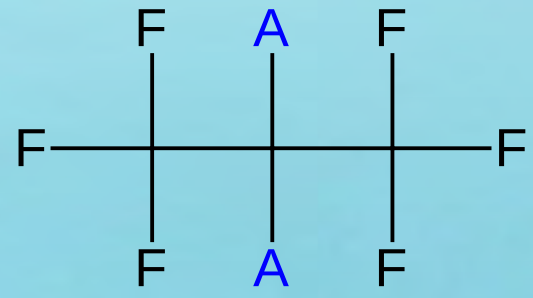


How PFAS have been defined by EPA

- Three substructures
  - Over 11,000 structures in Dashboard
  - R-(CF2)-CF(R')R", where both the CF2 and CF moieties are saturated carbons
  - R-CF20CF2-R', where R and R′ can either be F, O, or saturated carbons
  - CF3C(CF3)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

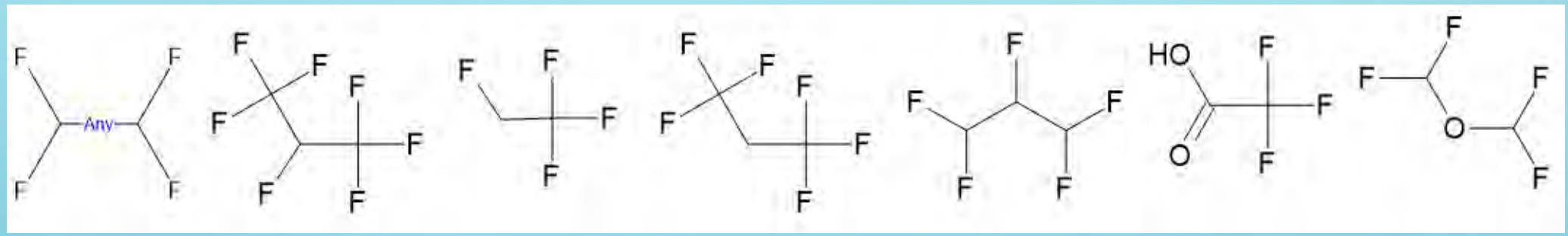






How PFAS have been defined by EPA

- 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

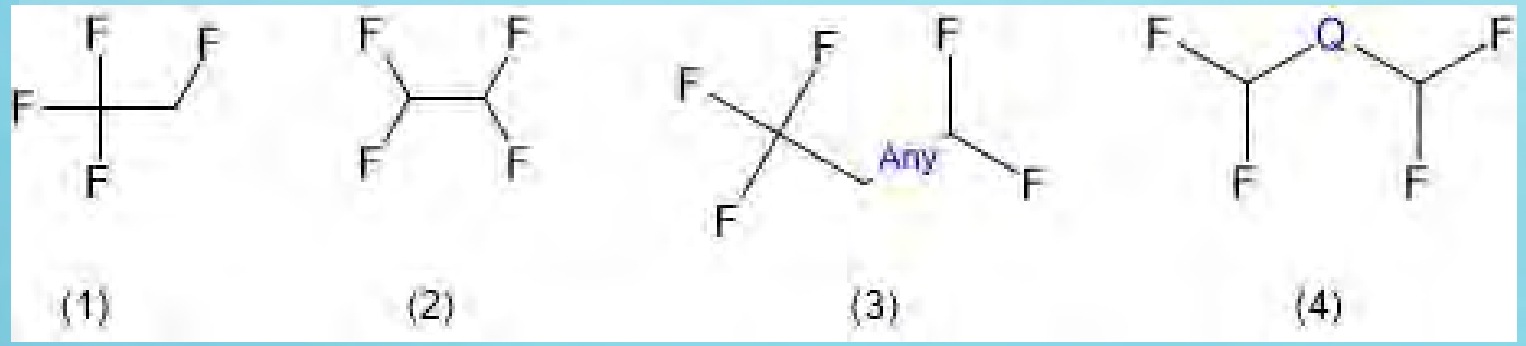


Refining Dashboard PFAS structures list

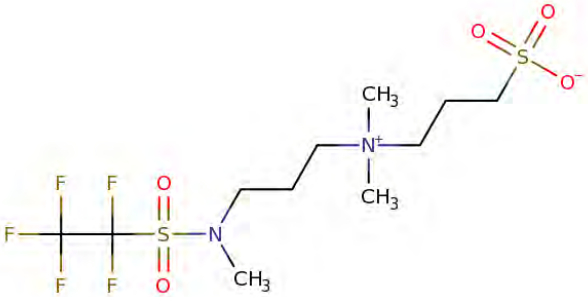
- In comparing various PFAS definitions, Dashboard PFAS structures list needed additional substructures
  - Structures were on TSCA 2021 list not on Dashboard list
  - Some highly branched or otherwise complex structures also not captured
- Compared structures on TSCA or OECD lists but not Dashboard 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 a 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

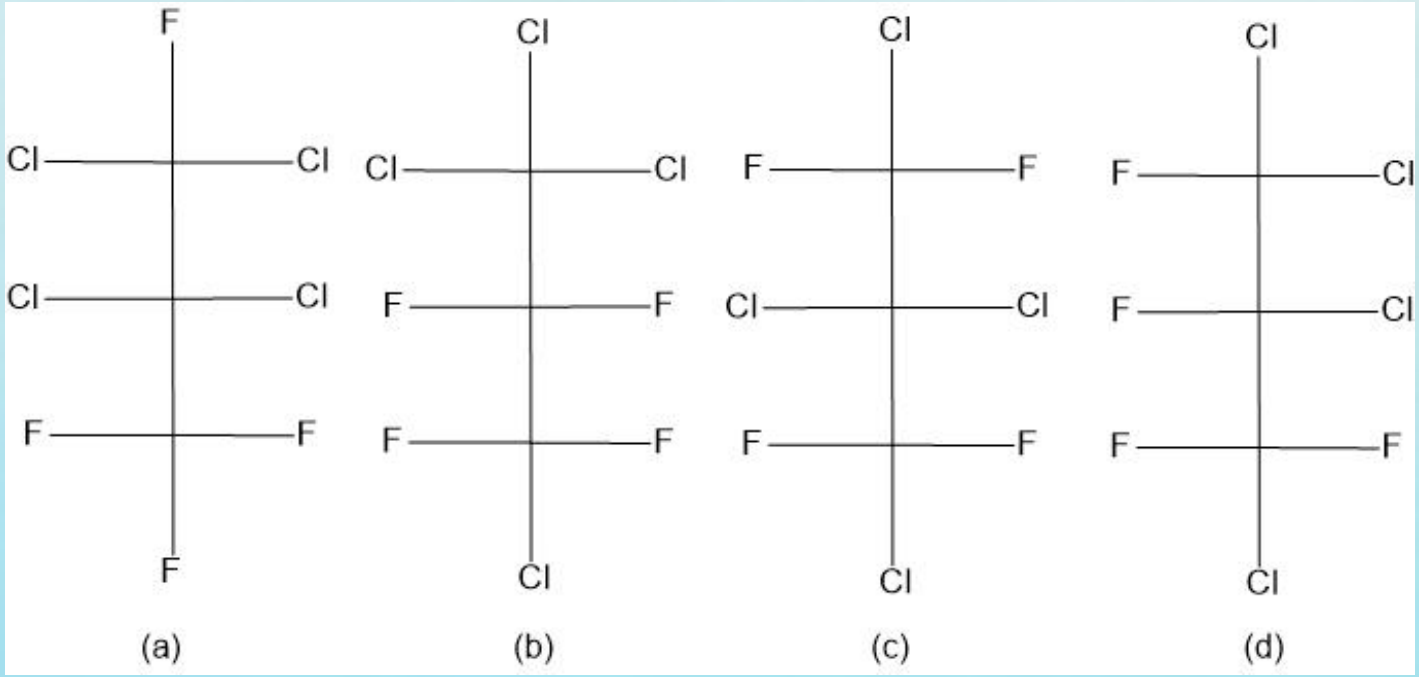


Definition complications

- 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

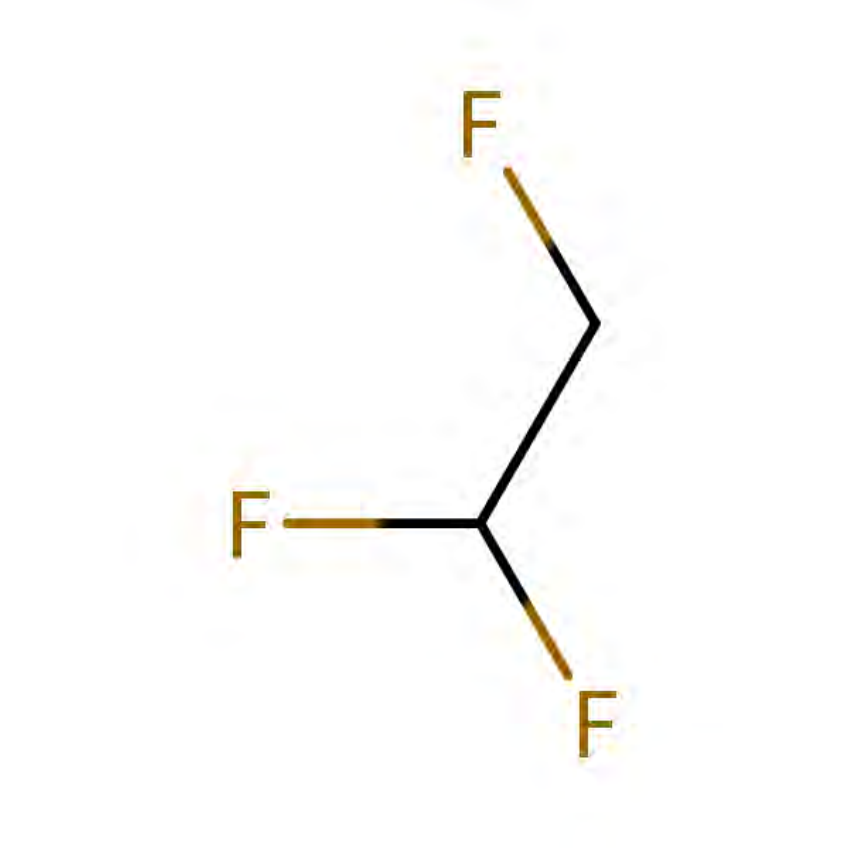
$C_3Cl_4F_4$



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

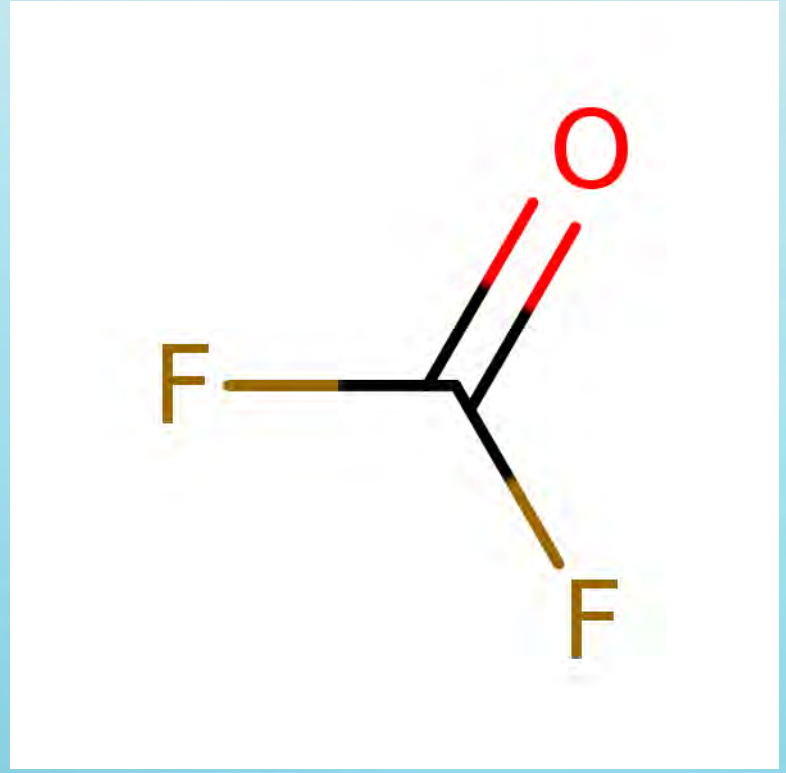


PFAS?

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

Maybe, Maybe Not PFAS – Terminal C

Carbonyl difluoride
(Fluorophosgene)

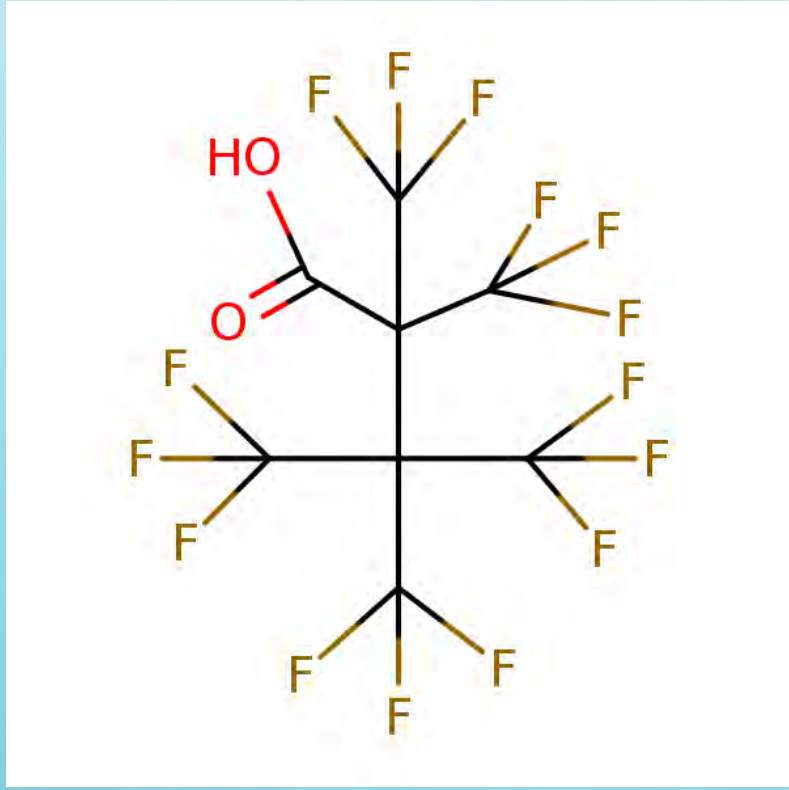


PFAS?

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

Maybe, Maybe Not PFAS – Branching

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

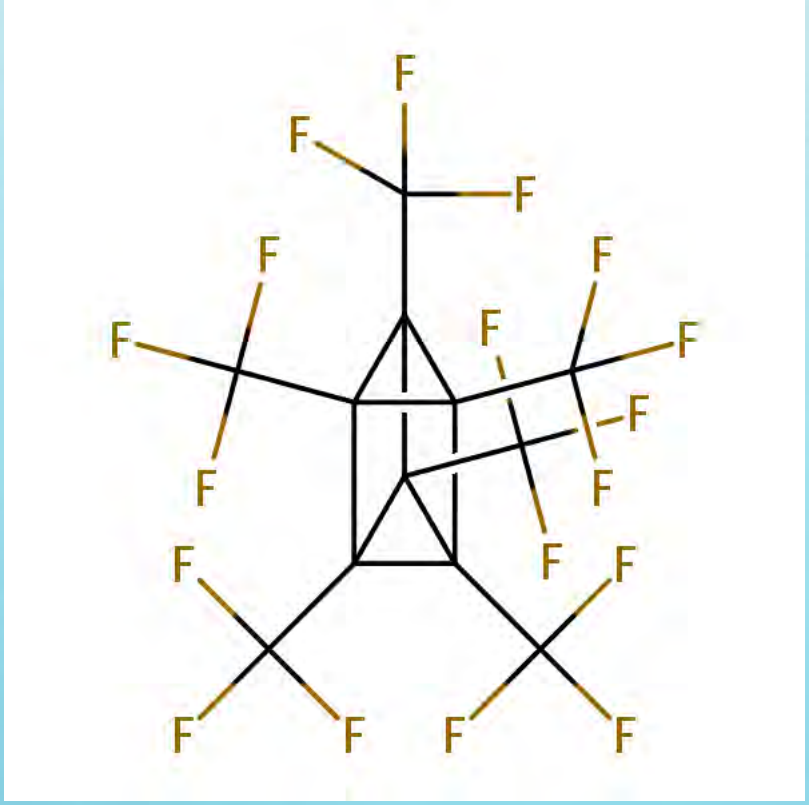


PFAS?

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

Maybe, Maybe Not PFAS – Branching

Perfluorohexamethylprismane

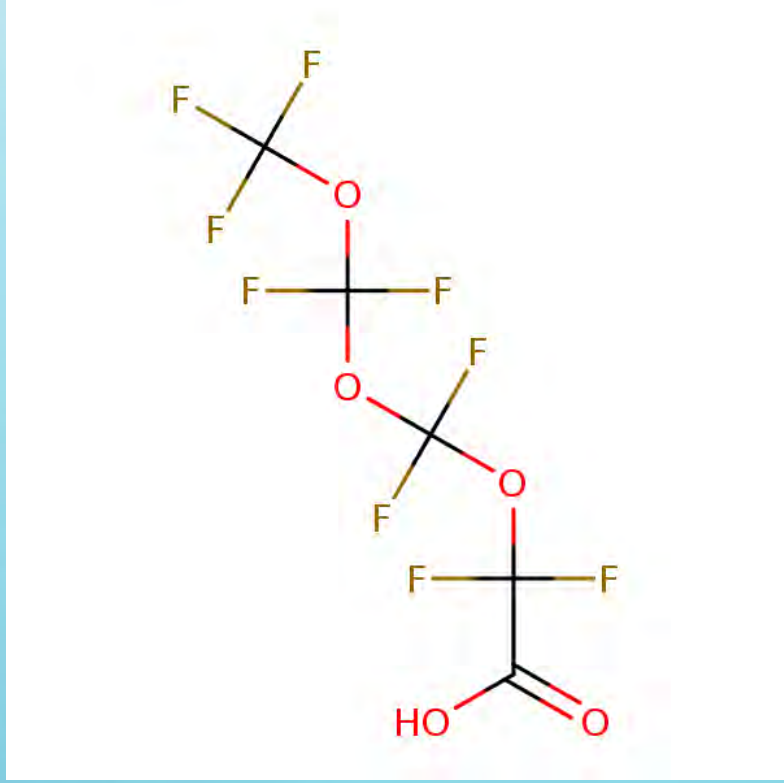


PFAS?

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

Maybe, Maybe Not PFAS – Ethers

Perfluoro-3,5,7-trioxaoctanoic acid

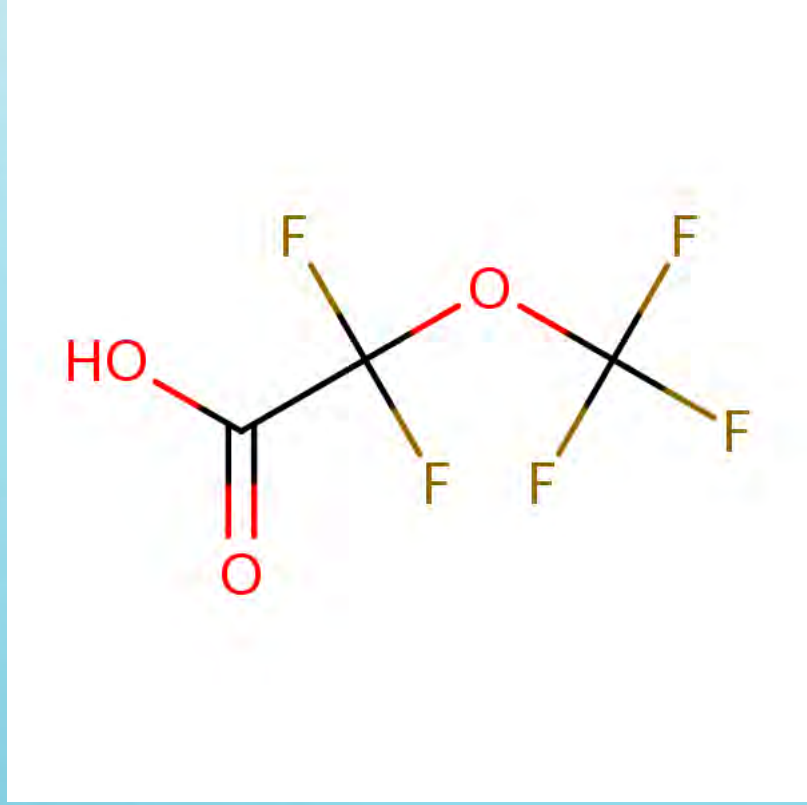


PFAS?

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

Maybe, Maybe Not PFAS – Ethers

Perfluoro-2-methoxyacetic acid

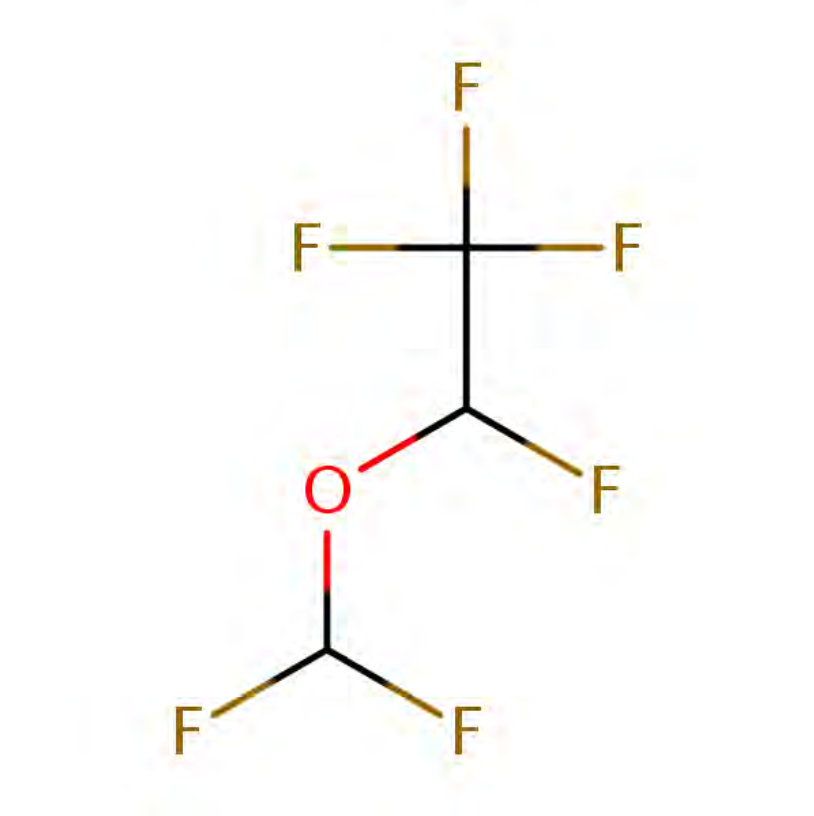


PFAS?

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

Maybe, Maybe Not PFAS – Ethers

Desflurane



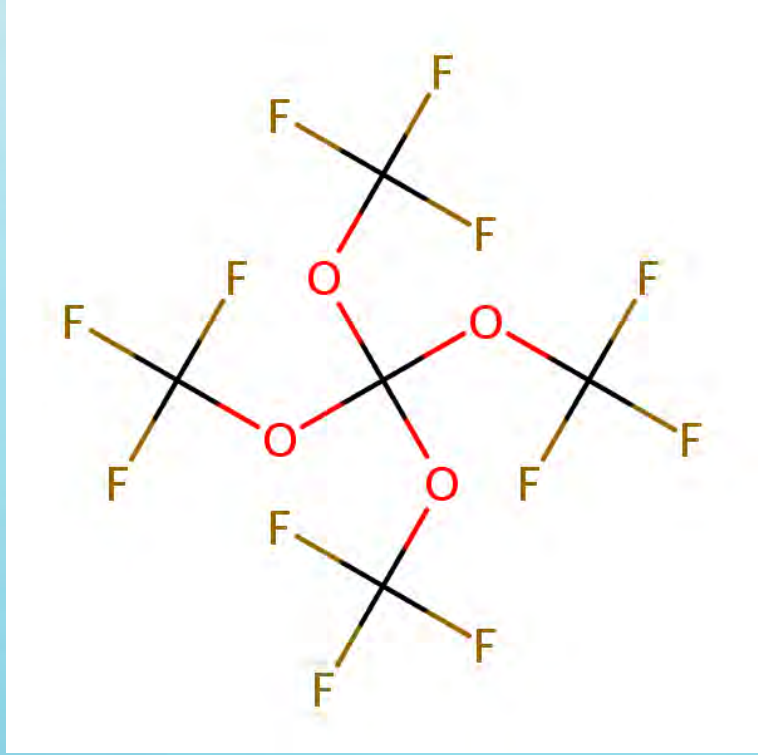
PFAS?

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

FDA approved drug for maintenance of general anesthesia

Maybe, Maybe Not PFAS – Ethers

Tetrakis(trifluoromethoxy)methane

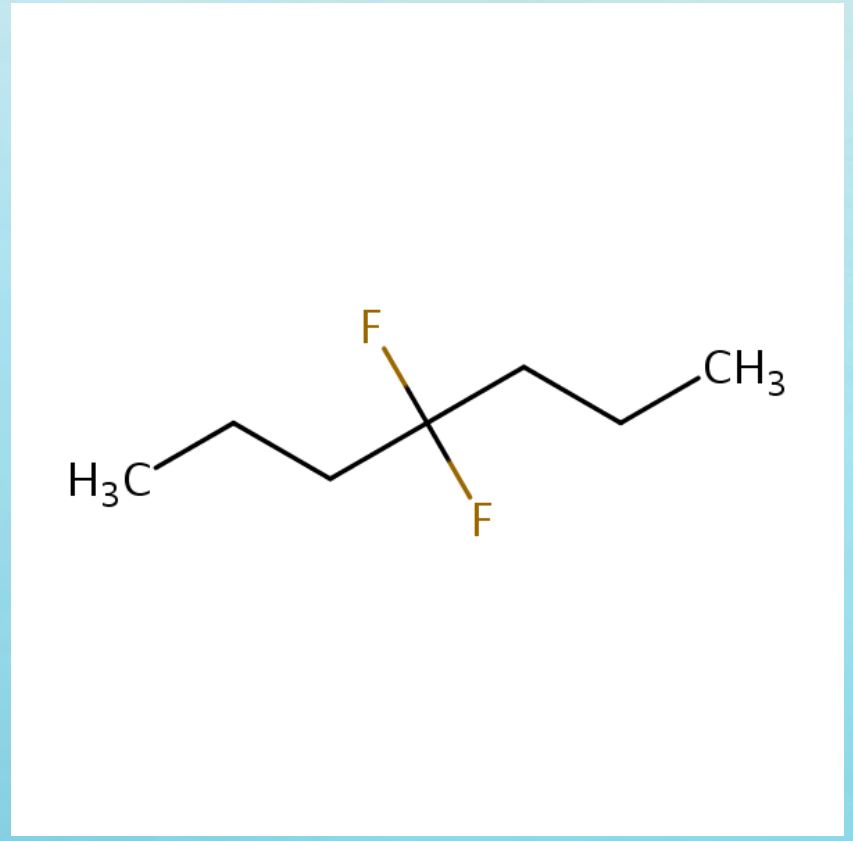


PFAS?

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

Maybe, Maybe Not PFAS – One CF2

4,4-Difluoroheptane

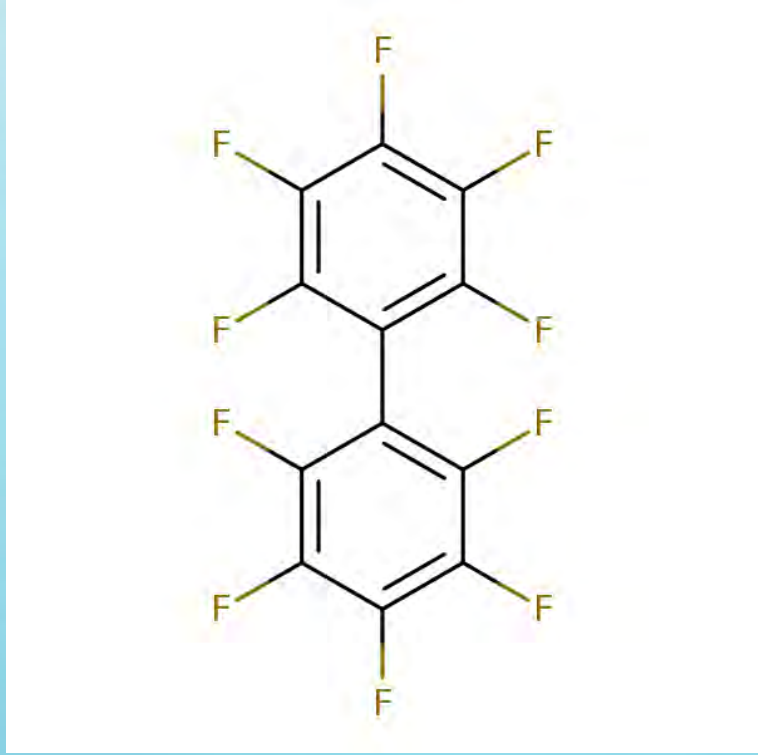


PFAS?

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

Maybe, Maybe Not PFAS – Aromatic

Perfluorobiphenyl



PFAS?

Definition	PFAS?
OECD	No
OW/OCSPP 2021	No
PFASSTRUCTv5	Yes
OW 2022	No
OCSPP 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