SAND2013-5845C

Degradation of Organophosphates

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Outline

- Background
- Testing
- Sandia Decon Foam
- Mutant Enzymes
- Polyoxoniobates
- Summary
- Acknowledgements

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What are organophosphates?

An **organophosphate** is the general name for esters of phosphoric acid.

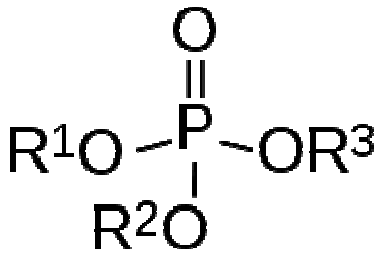
- widely used in both natural and synthetic compounds due to the ease with which organic groups can be linked together, e.g. esterification

Organophosphates and Agriculture

- Pesticides and Insecticides
- Irreversibly inactivate acetylcholinesterase enzyme
- Degradation by hydrolysis on exposure to sunlight, air, and soil,
  - degrade faster than the organochlorides pesticides
- Small amounts can still be detected in food and drinking water
- Even at low levels, can be hazardous and cause irreversible damage

Applications of Organophosphates

- Insecticides (*e.g. Malathion, Parathion*)
- Herbicides (*e.g. DEF*)
- Chemical Nerve Agents (*e.g. Sarin, VX*)
- Flame Retardents (*e.g. TDCPP*)
- Also found in DNA/RNA Backbones



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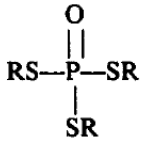
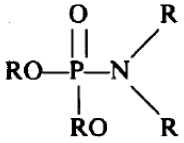
Types of Organophosphates

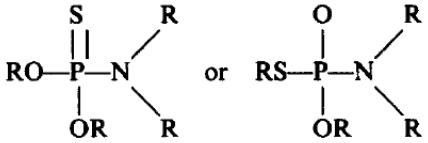
Phosphorotrithioates



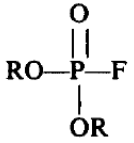
Phosphoramidates



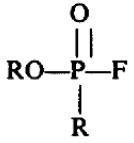
Phosphoramidothioates



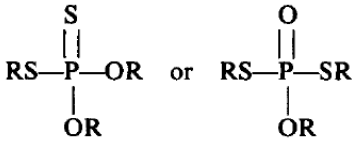
Phosphorofluoridates



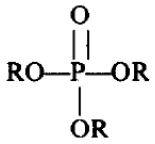
Phosphonofluoridates



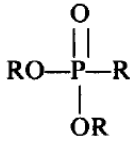
Phosphorodithioates



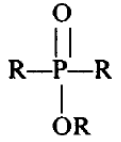
Phosphates



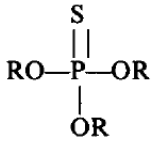
Phosphonates



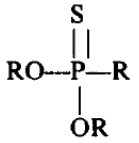
Phosphinates



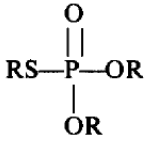
Phosphorothioates (S=)



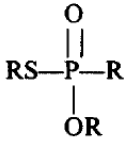
Phosphonothioates (S=)



Phosphorothioates (S-substituted)



Phosphonothioates (S-substituted)



Marrs, T. C. Pharmacology & Therapeutics 1993, 58, 1, 51.

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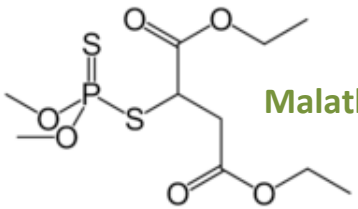
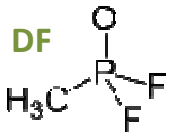
Organophosphate Chemicals


Malathion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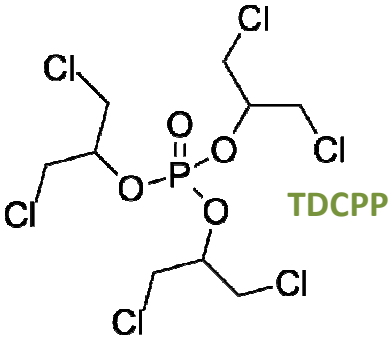
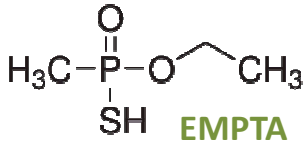
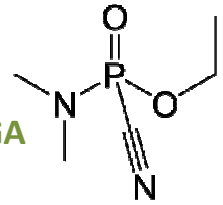

TDCPP


EMPTA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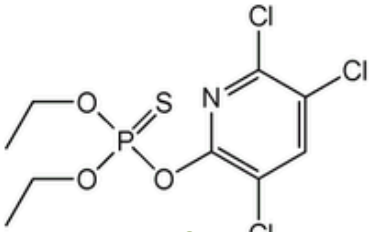
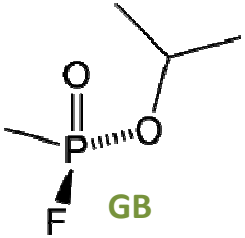

Chlorpyrifos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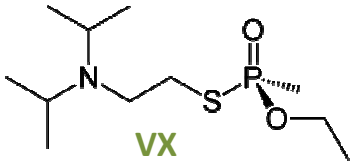
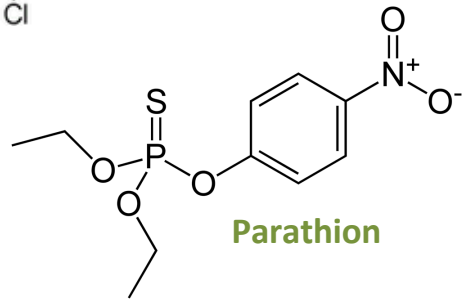
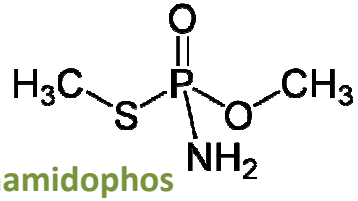
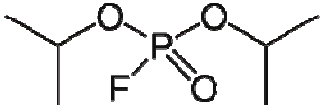
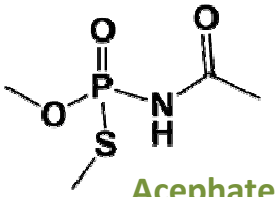
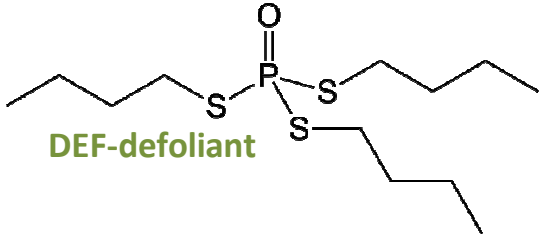

VX


Parathion


Methamidophos


DFP


Acephate


DEF-defoliant

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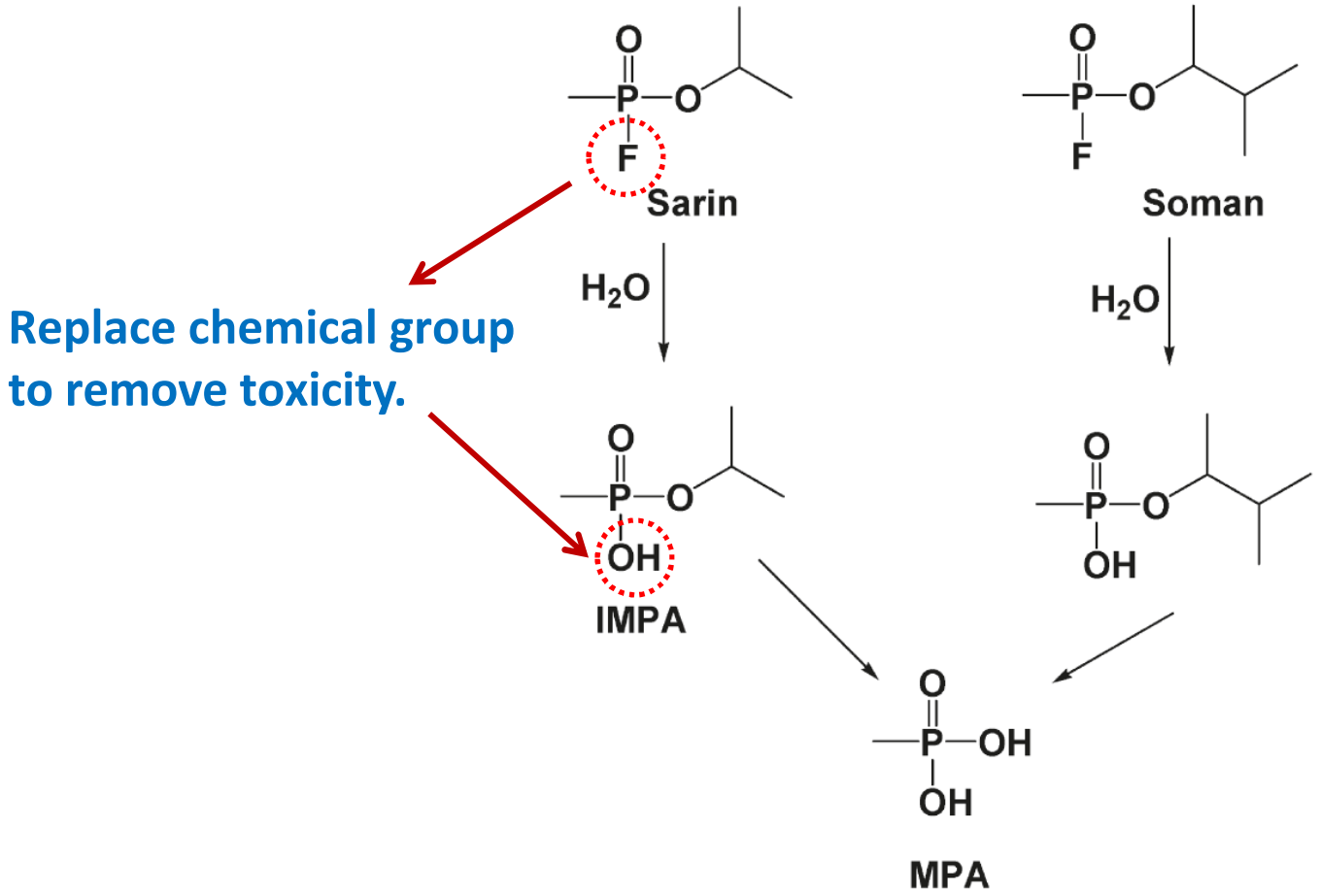
Mechanism for Degradation



Kim, K.; Tsay, O. G.; Atwood, D. A.; Churchill, D. G. Chem. Rev. 2011, 111, 9, 5345.

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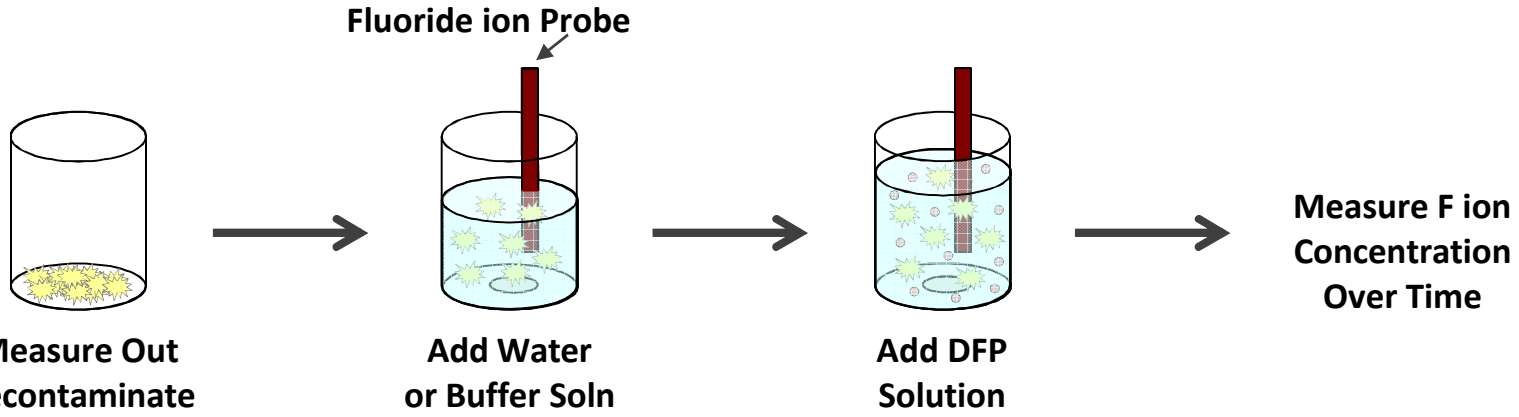
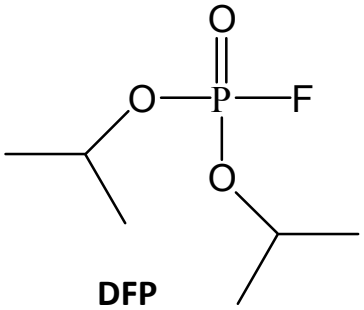
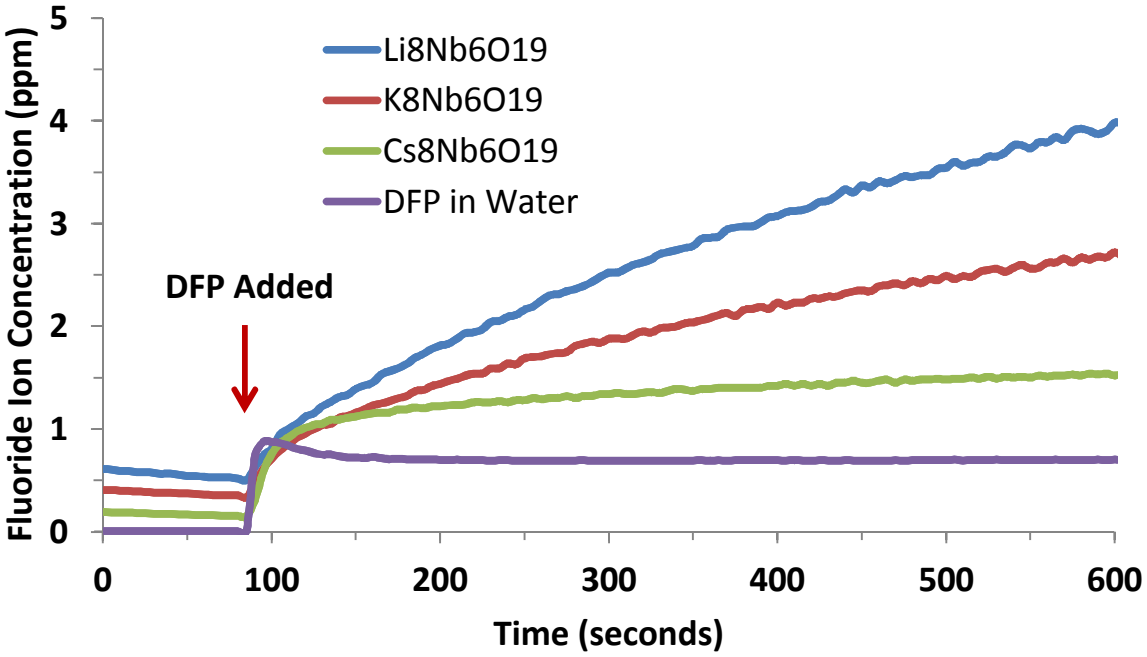
Testing (F- probe) a Material for Decontamination Potential







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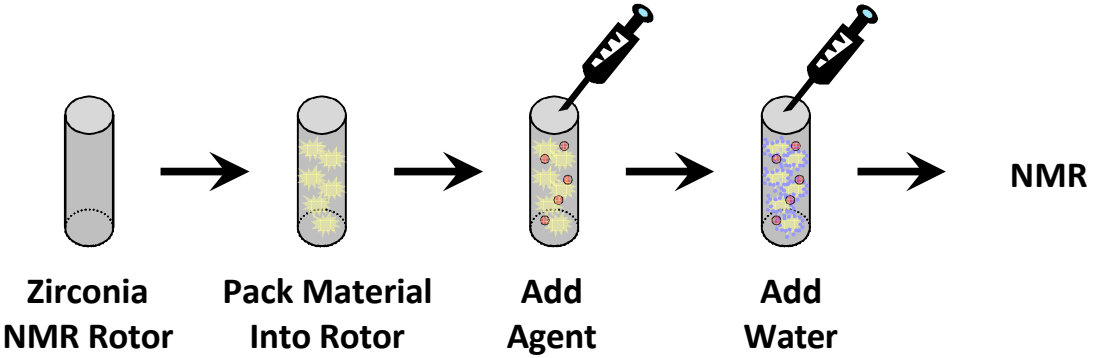
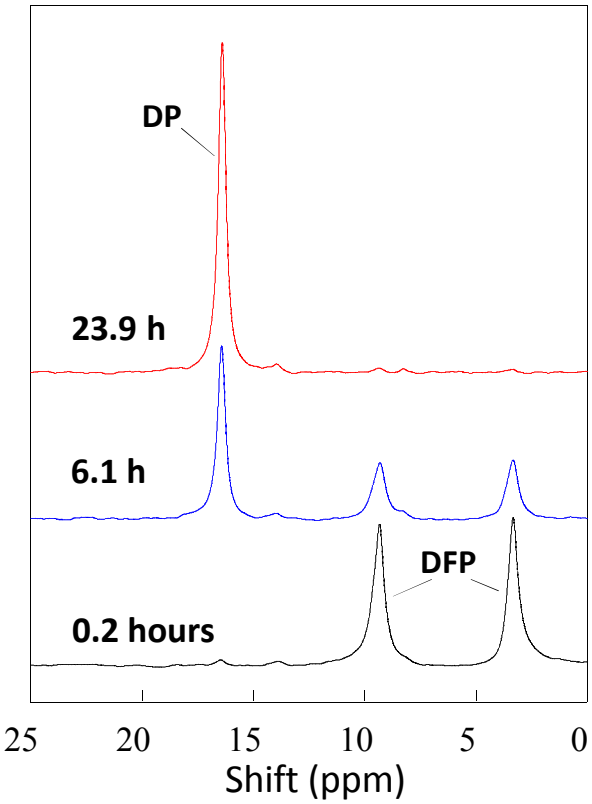
Testing (NMR) a Material for Decontamination Activity

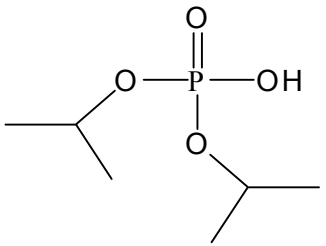


In the ^{31}P NMR, DFP signal goes down as the degradation product DP forms.

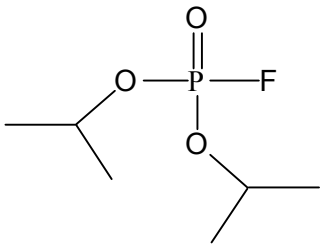


Diisopropyl Phosphate (DP)

Degraded Product



Diisopropyl Fluorophosphate (DFP)



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What is DF-200?

Ingredients

- Surfactants
- Solvents
- Buffers
- Peroxide (7.5% Soln)
- Novel Activator

Synergistic Formulation

(*contains multiple reactive species*)

- Spray
- Foam
- Aerosol

Neutralize

- Biological Agents
- Biological Pathogens
- Chemical Agents
- Toxic Industrial Chemicals
- Pesticides

Final peroxide concentration is ~3.6%

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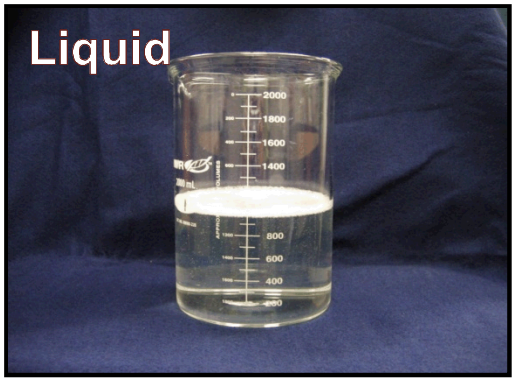
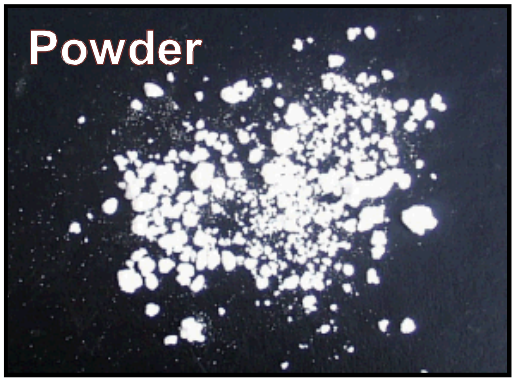
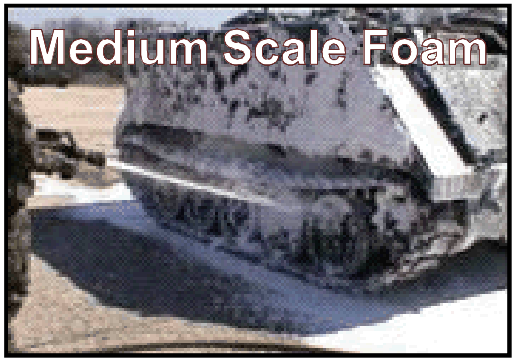
Sandia Decon Foam Deployment Methods







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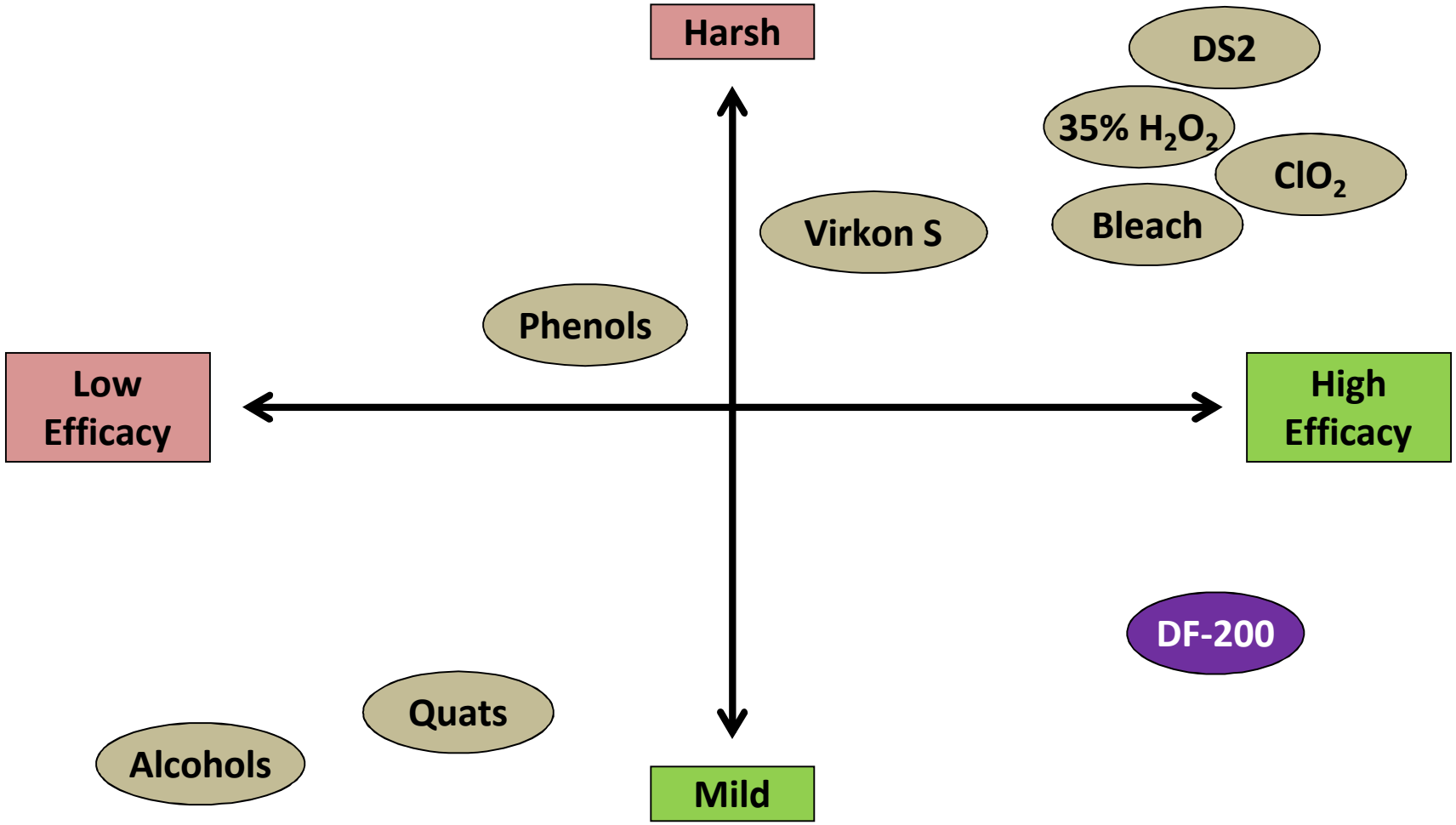
Decontaminant Comparison



The Sandia Decon Foam technology (DF-200) was designed to be a broad spectrum decontaminant

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Corrosion Comparisons

Steel Coupons

Deionized Water

24 Hour Exposure

Sandia Decon Foam

24 Hour Exposure

Bleach

24 Hour Exposure

The Sandia Decon Foam technology (DF-200) was developed as an alternative to harsh formulations such as bleach or DS2

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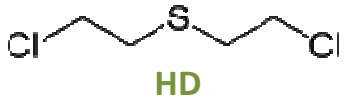
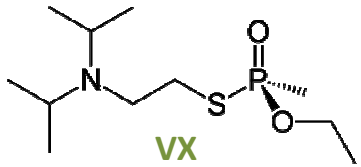
Decon Data

Decontaminant	HD		VX		GD	
	10 min	60 min	10 min	60 min	10 min	60 min
DS2	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
DF-200	69	>99.9	>99.9	>99.9	>99.9	>99.9
GD5	87	>99.9	99	>99.9	>99.9	>99.9
L-Gel 115	99	>99.9	>99.9	>99.9	20	55
BX-24	>99.9	>99.9	50	50	8	55
CASCAD	70	80	>99.9	>99.9	25	55
German Emulsion	80	85	20	20	>99.9	>99.9
Enzyme	15	30	0	0	50	60
ECASOL	0	0	0	0	<5	30

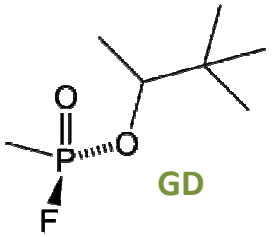
Percent decontamination from kinetic tests in stirred reactors with a 50:1 (*decon:agent*) challenge ratio.



HD



VX



GD

DoD RestOps ACTD Data from Early 2000s

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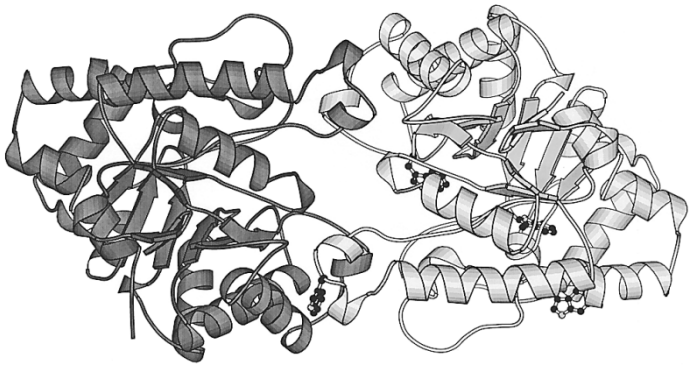
Cell-free Translation of Rational OPH Mutants

Advantages of Cell-free Approach:

- Faster, less expensive than traditional cellular-based methods
- Proteins can be made directly from PCR templates, eliminating costly, time-consuming steps for plasmid cloning
- Multiple conditions can be screened simultaneously
- Multiple proteins can be expressed simultaneously in one reaction to facilitate production of active protein complexes
- Proteins can be characterized directly from the translation reactions.



Ribbon drawing of OPH

Biochemistry, 1997, 36 (47), pp 14366–14374

CFS GenDecoder Robot

Produces 384 proteins/day

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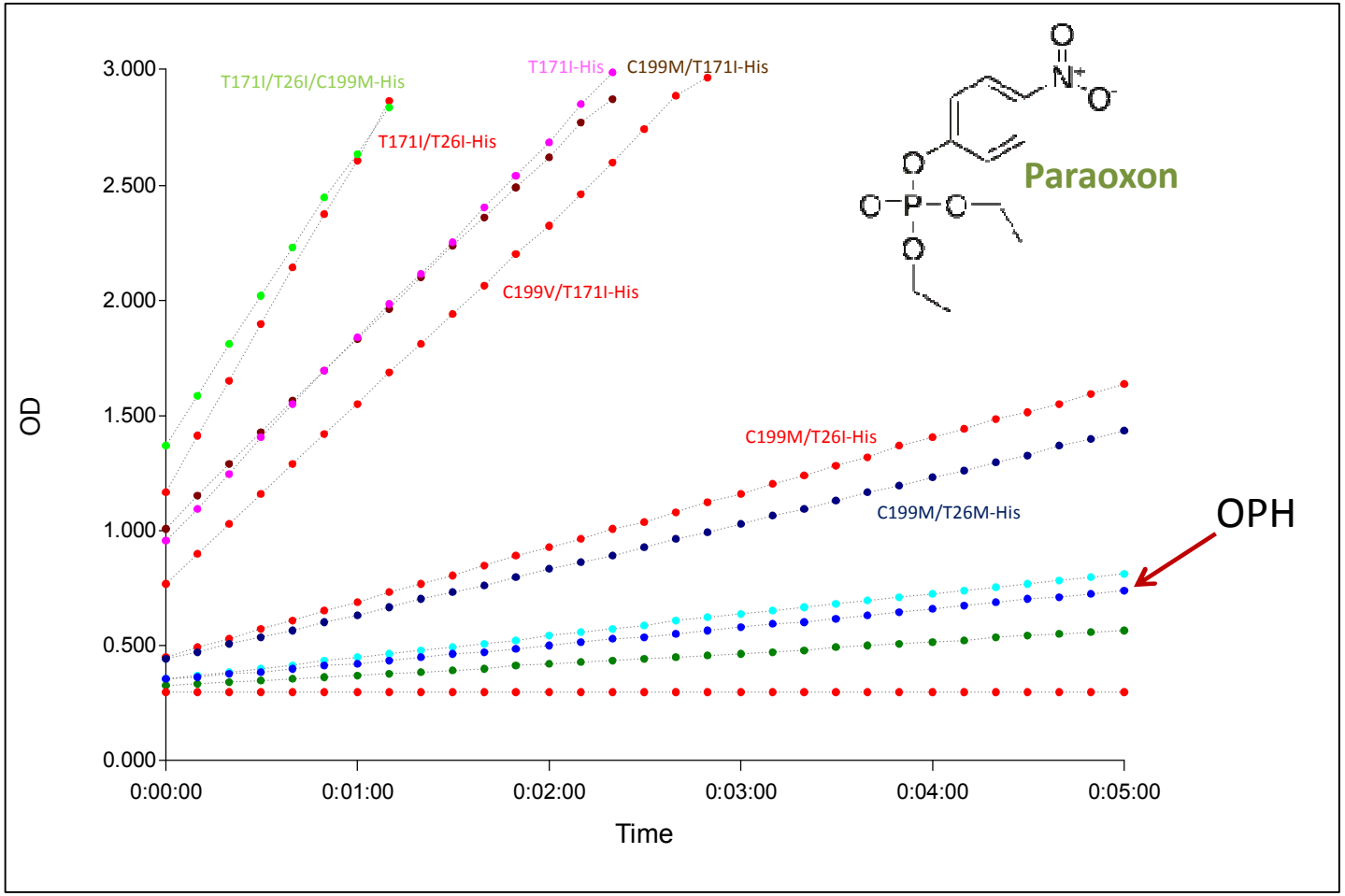
Paraoxon Activity Assays for Some Rational Mutants



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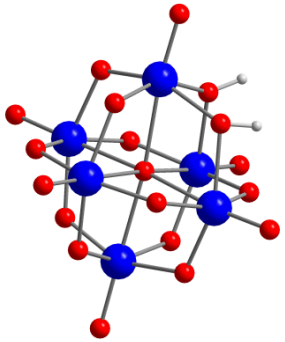
Polyoxoniobates

Purpose: Use polyoxoniobates (PONb) to decontaminate organophosphate compounds.

What are PONb:

- an alkaline class of polyoxometalates.
- a small metal-ion cluster.



$Nb_6O_{19}^{8-}$

Counter cation: Li, K, or Cs
$Li_8Nb_6O_{19}$
$K_8Nb_6O_{19}$
$Cs_8Nb_6O_{19}$

PONb:

- have high solubility in water.
- are entirely inorganic.
- are easily synthesized in one step.
- exhibit their own solution buffering.

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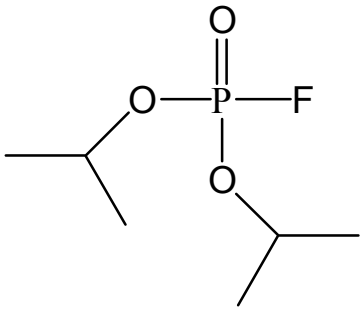
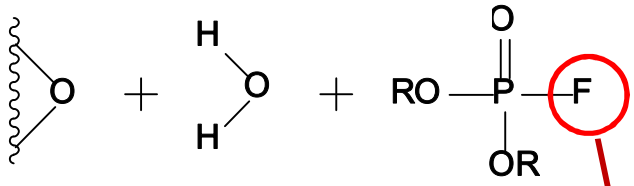
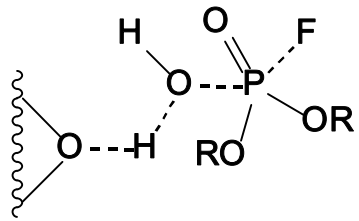
PONb Decontamination Mechanism

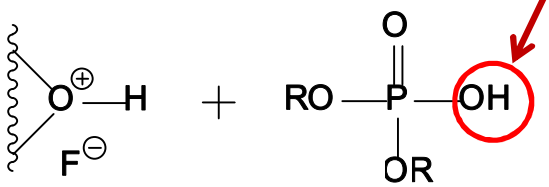


Diisopropyl Fluorophosphate (DFP)



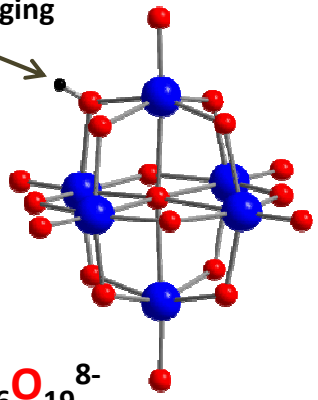


Replace chemical group to remove toxicity.



R = *isopropyl group*

protonated μ_2 bridging oxo-ligand



$Nb_6O_{19}^{8-}$

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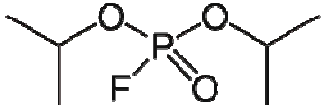
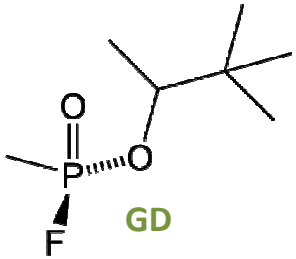
Reaction Kinetics

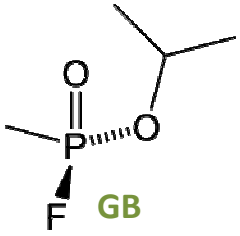
Material	OP	Measurement (type)	Mole Ratio (OP:PONb)	RXN Volume (mL)	k_{obs} (s^{-1})	$t_{1/2}$ (h), *(s)
$Li_8Nb_6O_{19}$	DFP	Ion Probe	3.6 ± 0.3	10.	$6.0 \times 10^{-5} \pm 0.8 \times 10^{-5}$	3.2 ± 0.4
$K_8Nb_6O_{19}$	DFP	Ion Probe	4.8 ± 0.5	10.	$3.4 \times 10^{-5} \pm 0.3 \times 10^{-5}$	5.7 ± 0.4
$Cs_8Nb_6O_{19}$	DFP	Ion Probe	4.4 ± 0.2	10.	$8.3 \times 10^{-6} \pm 3 \times 10^{-6}$	27 ± 13
$Li_8Nb_6O_{19}$	DFP	NMR	2.2	0.10	1.6×10^{-5}	12
$K_8Nb_6O_{19}$	DFP	NMR	2.1	0.10	2.3×10^{-5}	8.5
$Cs_8Nb_6O_{19}$	DFP	NMR	2.3	0.10	1.8×10^{-5}	11
$Li_8Nb_6O_{19}$	GD	NMR	0.39	0.32	1.5×10^{-3}	0.13
$Li_8Nb_6O_{19}$	GD	NMR	4.3	0.32	2.5×10^{-4}	0.77
$Li_8Nb_6O_{19}$	GD	NMR	17	0.32	1.8×10^{-4}	1.1
$Li_8Nb_6O_{19}$	GB	NMR	1.6	0.32	4.4×10^{-2}	16*
$K_8Nb_6O_{19}$	GB	NMR	1.6	0.32	3.9×10^{-3}	180*
$Cs_8Nb_6O_{19}$	GB	NMR	1.0	0.32	5.3×10^{-3}	130*
$Li_8Nb_6O_{19}$	VX	NMR	1.0	0.32	7.4×10^{-6}	26
$K_8Nb_6O_{19}$	VX	NMR	1.0	0.32	2.8×10^{-5}	6.9
$Cs_8Nb_6O_{19}$	VX	NMR	1.0	0.32	3.6×10^{-5}	5.4



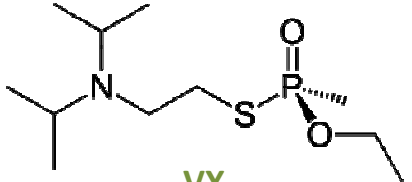
DFP



GD



GB



VX

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Comparison of PONbs to Literature

Challenges associated with comparing data to prior reported studies include:

1. Differences in analytical techniques.
2. Differences in CWAs and/or simulants.
3. Different molar ratios of CWA and/or simulant to the neutralization catalyst.

In particular, many previous studies have used much lower ratios of CWA to decontamination agent. For this study, a choice was made to study high molar ratios due to the future application of the PONbs on fabric.

Examples

1. Polyacrylamidoxime (PANOx) for the neutralization of GD. The kinetic observations for k_{obs} and $t_{½}$ are $3.6e^{-4}$ s^{-1} and 0.54 hours, respectively.
2. Breakdown of GD using $Zr(OH)_4$ in which $t_{½}$ is reported to be 0.15 hours.

Neutralization catalyst ranged from approximately 0.01 to 0.02.

Our results were obtained with mole ratios of 0.39, 4.3, and 17.

Minimum of 20 times greater than other reports in the literature.

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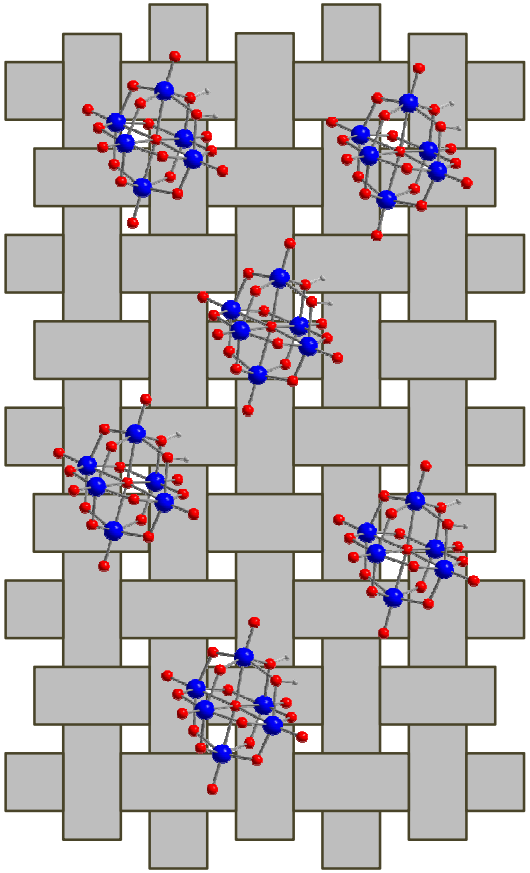
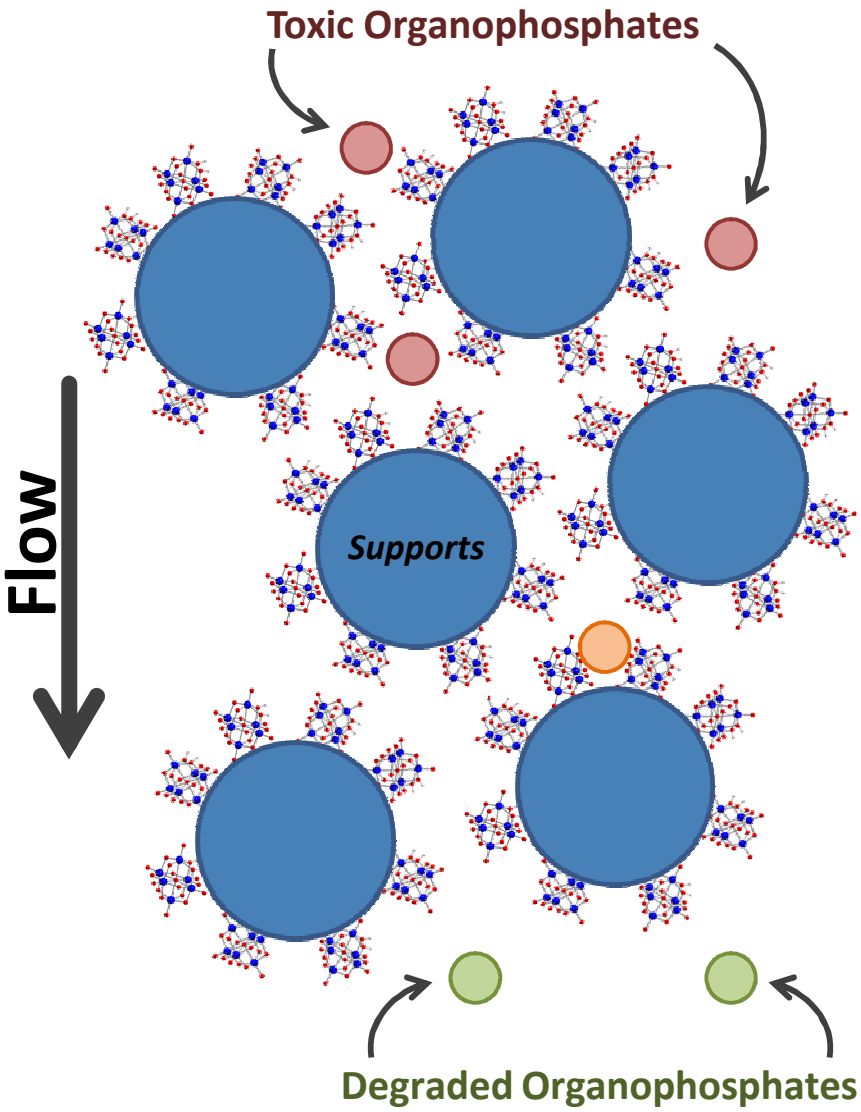
Applications of PONbs

Examples not drawn to scale.



Attachment to Fabrics



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Summary

- **Decon Foam**
  - Environmentally friendly
  - Deployable as liquid, foam, spray, and aerosol
  - Broad spectrum
- **Mutant Enzymes**
  - Proteins are made directly from PCR templates
  - Faster, less expensive option compared to cellular-based methods
  - Significantly faster kinetics than OPH
- **Polyoxoniobates**
  - Rapid neutralization
  - Can be attached to surfaces
  - Catalytic/Inorganic

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Acknowledgements

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OF THE NATIONAL ACADEMIES

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