Electronic Supplementary Material (ESI) for Environmental Science: Advances.

Chemometric Modeling of Lowest Observed Effect Level (LOEL) and No Observed Effect Level (NOEL) for Rat Toxicity

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Supplementary Information SI-2

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Materials and methods

Definition of different statistical parameters

$$R^2 = 1 - \frac{\Sigma\left(Y_{obs(train)} - Y_{calc(train)}\right)^2}{\Sigma\left(Y_{obs(train)} - \overline{Y}_{train}\right)^2}$$

$$Q^2_{LOO} = 1 - \frac{\Sigma\left(Y_{obs(train)} - Y_{calc(train)}\right)^2}{\Sigma\left(Y_{obs(train)} - \overline{Y}_{train}\right)^2}$$

Where, $R^2 =$ Co-efficient of determination

$Q^2_{LOO} =$ Cross-validated correlation coefficient

$Y_{obs(train)} =$ Observed response value of training set

$Y_{calc(train)} =$ Calculated response value of training set

$\overline{Y}_{train}$= Average of all responses of training set

$$Q^2_{F1} = 1 - \frac{\Sigma\left(Y_{obs(test)} - Y_{calc(test)}\right)^2}{\Sigma\left(Y_{obs(test)} - \overline{Y}_{train}\right)^2}$$

$$Q^2_{F2} = 1 - \frac{\Sigma\left(Y_{obs(test)} - Y_{calc(test)}\right)^2}{\Sigma\left(Y_{obs(test)} - \overline{Y}_{test}\right)^2}$$

Where, $Y_{obs(test)} =$ Observed response value of training set

$Y_{calc(test)} =$ Calculated response value of training set

$\overline{Y}_{train}$= Average of all response of training set

$\overline{Y}_{test}$= Average of all response of test set

Various PLS plot of different QSAR Models. A: Model IM1; B: Model IM2; C: Model IM3; D: Model IM4.

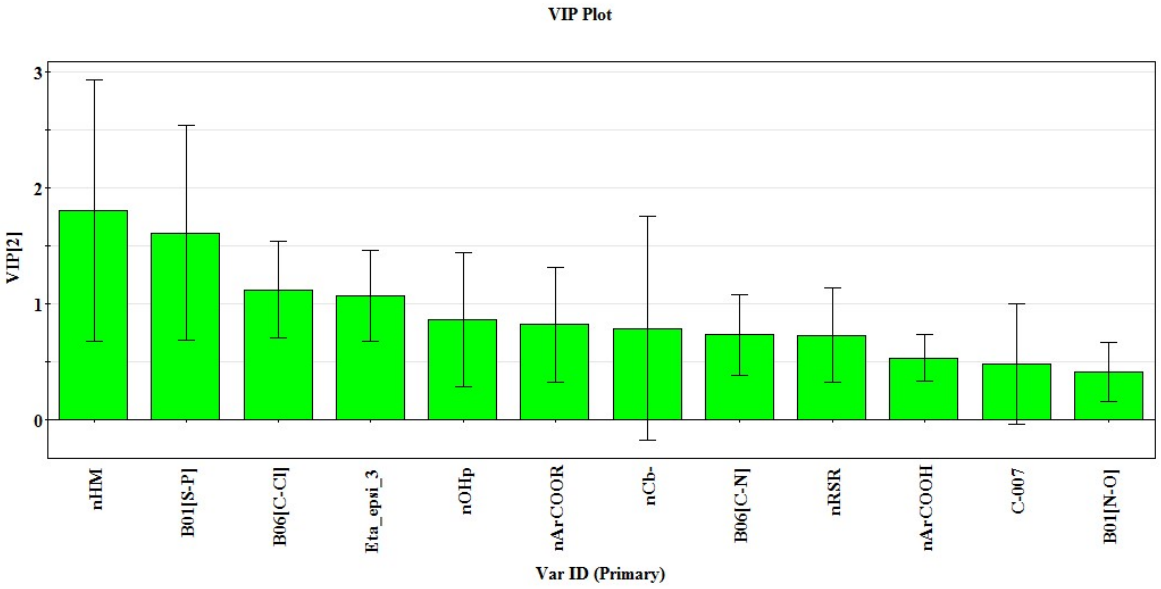

Fig.S1. VIP plot of Model IM1 (chronic Toxicity; pLOEL endpoint)

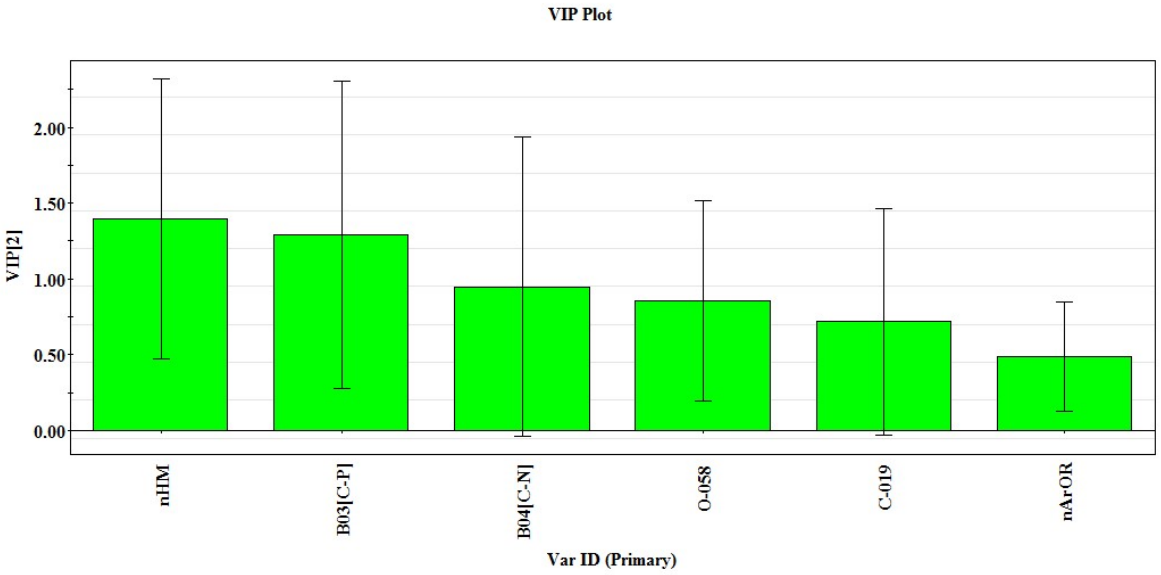

Fig.S2. VIP plot of Model IM2 (chronic Toxicity; pNOEL endpoint)

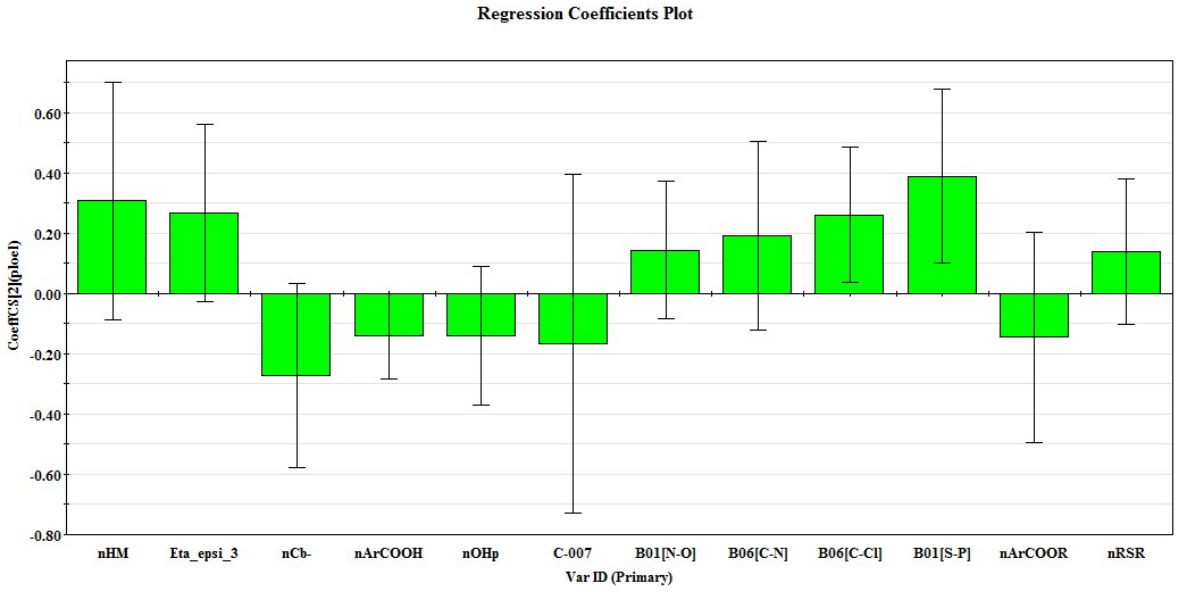

Fig.S3. Regression coefficient plot of Model IM1 (chronic Toxicity; pLOEL endpoint)

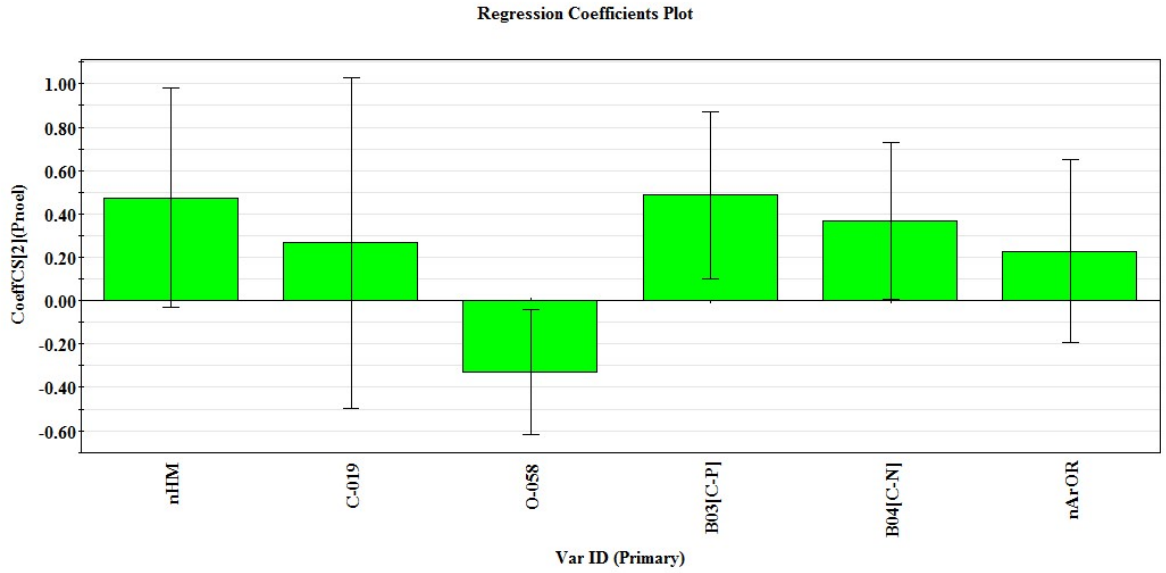

Fig.S4. Regression coefficient plot of Model IM2 (chronic Toxicity; pNOEL endpoint)

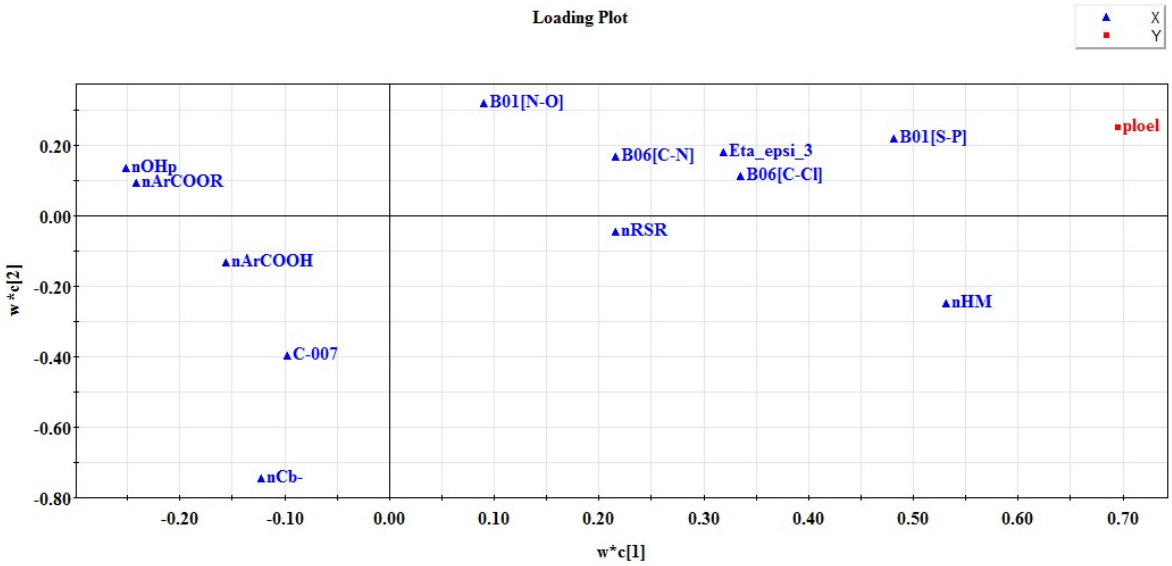

Fig.S5. Loading plot of Model IM1 (chronic Toxicity; pLOEL endpoint)

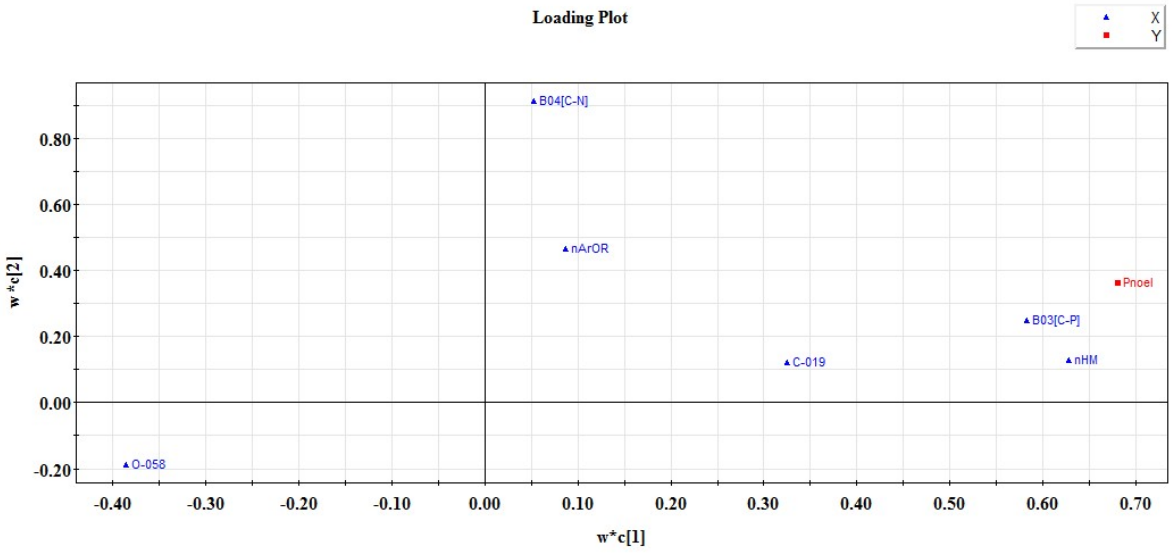

Fig.S6. Loading plot of Model IM2 (chronic Toxicity; pNOEL endpoint)

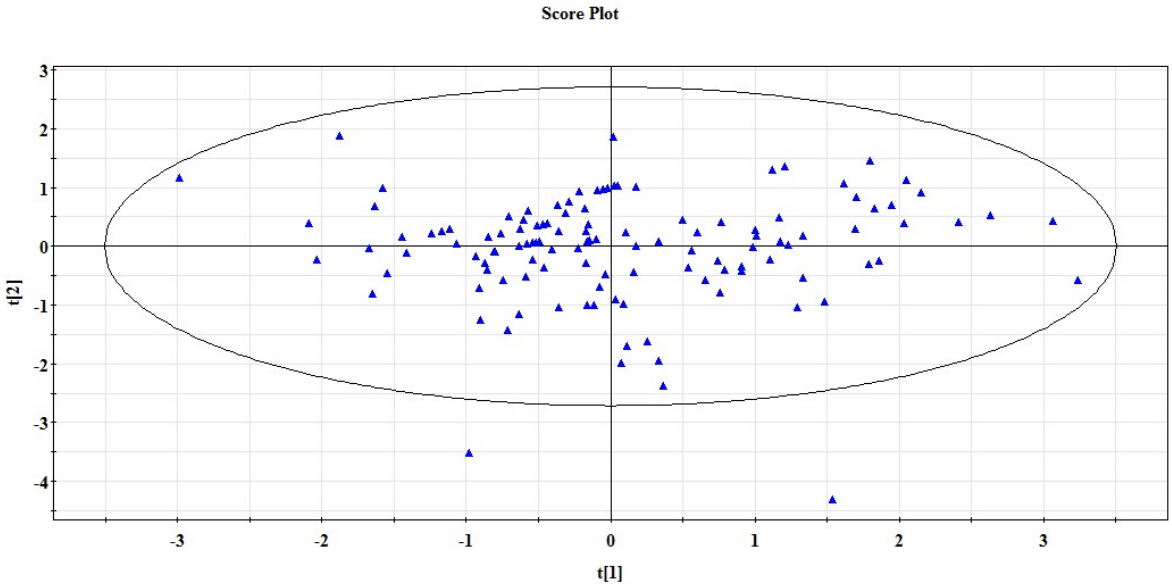

Fig.S7. Score plot of Model IM1 (chronic Toxicity; pLOEL endpoint)

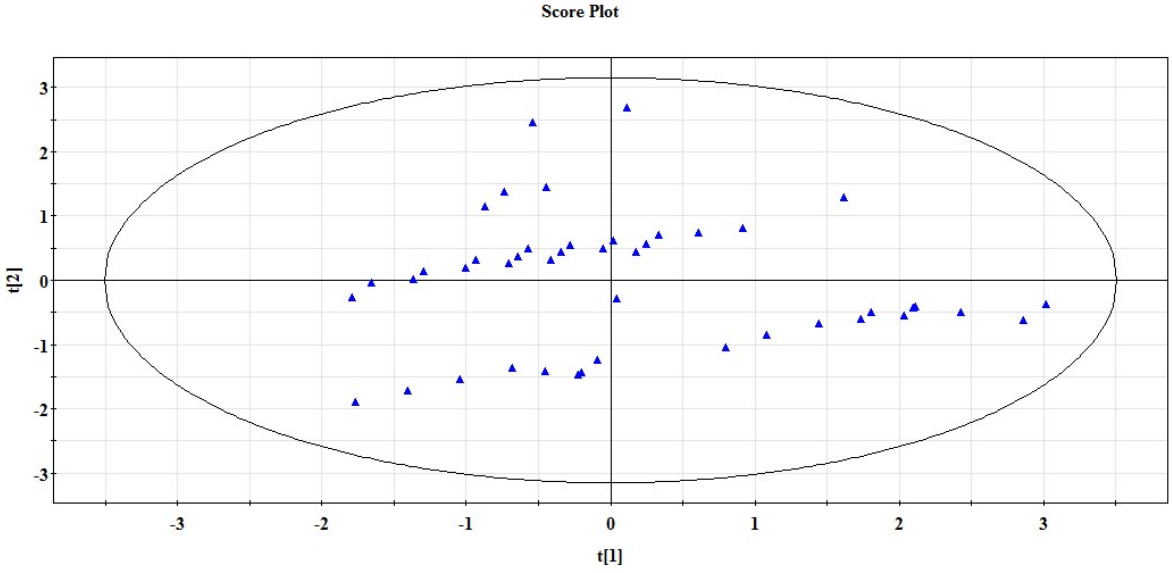

Fig.S8. Score plot of Model IM2 (chronic Toxicity; pNOEL endpoint)

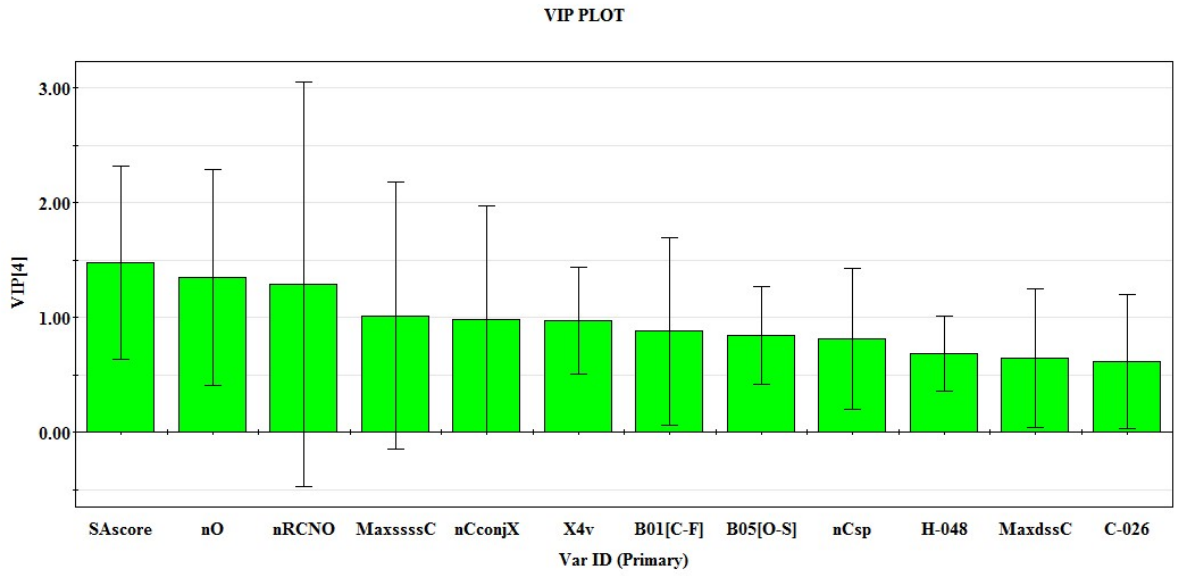

Fig.S9. VIP plot of Model IM3 (sub-chronic Toxicity; pLOEL endpoint)

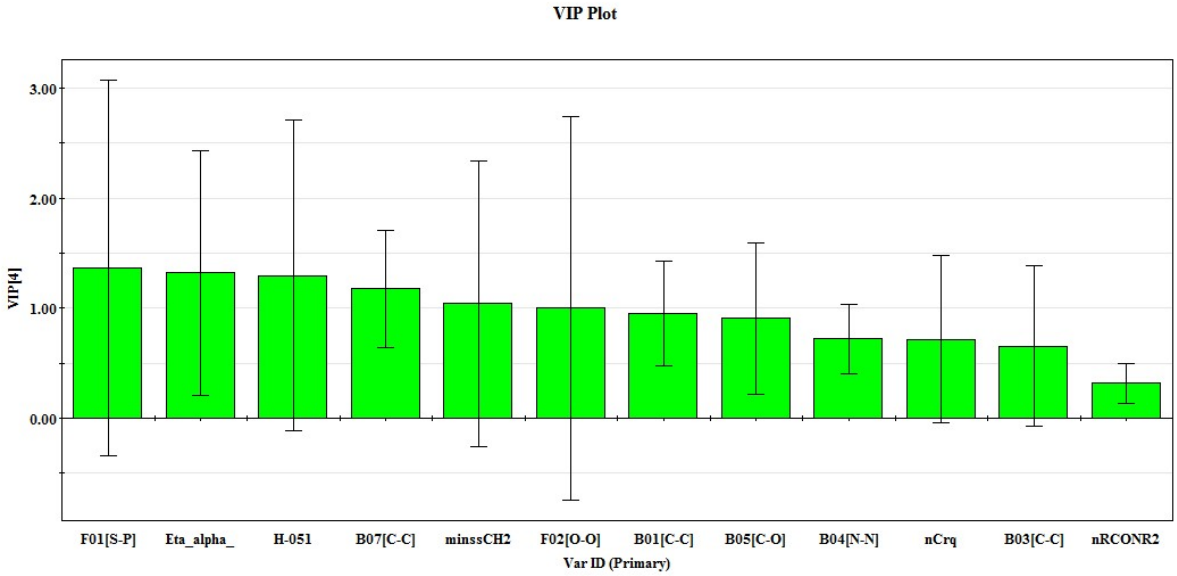

Fig.S10. VIP plot of Model IM4 (sub-chronic Toxicity; pNOEL endpoint)

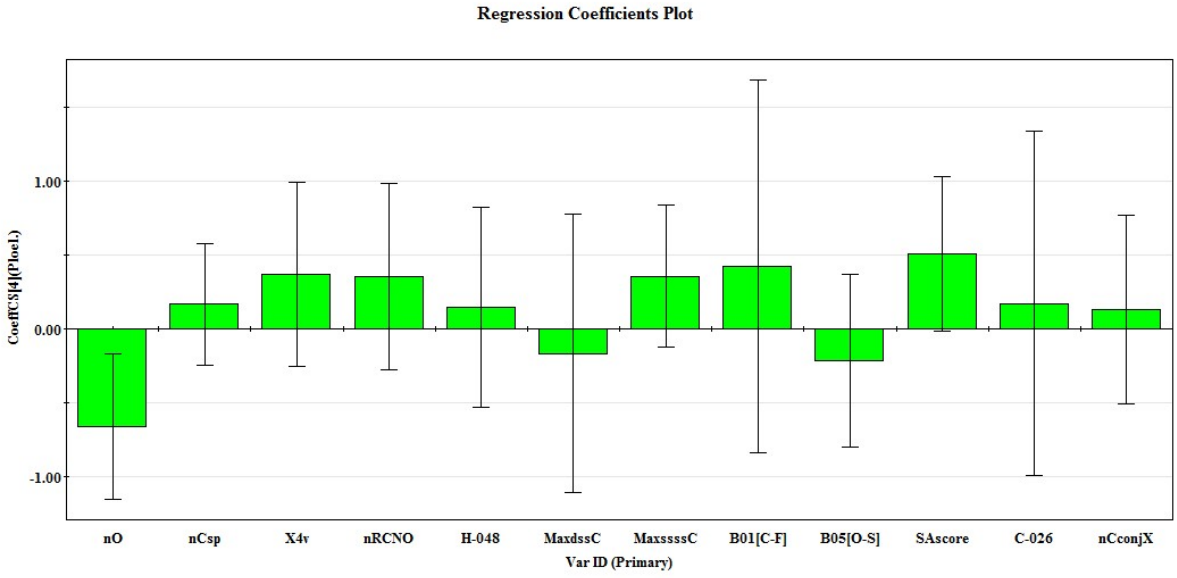

Fig.S11. Regression coefficient plot of Model IM3 (sub-chronic Toxicity; pLOEL endpoint)

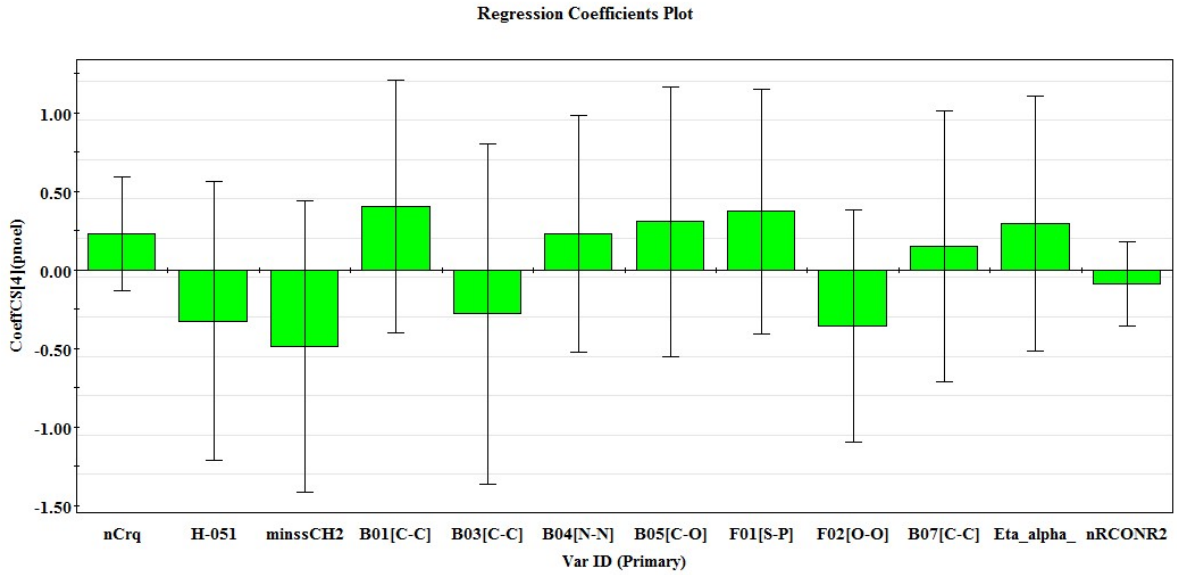

Fig.S12. Regression coefficient plot of Model IM4 (sub-chronic Toxicity; pNOEL endpoint)

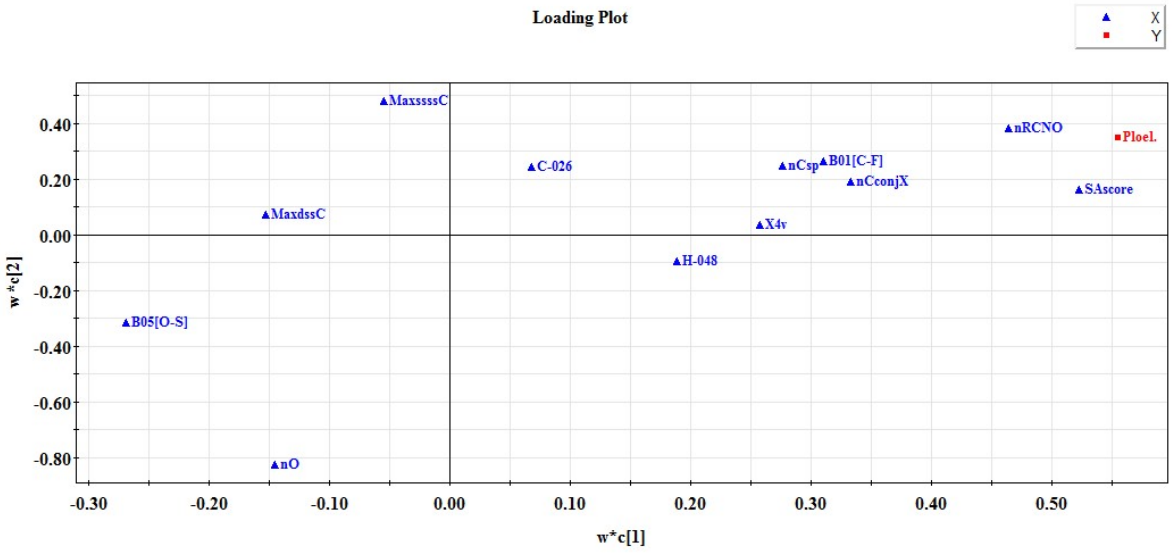

Fig.S13. Loading plot of Model IM3 (sub-chronic Toxicity; pLOEL endpoint)

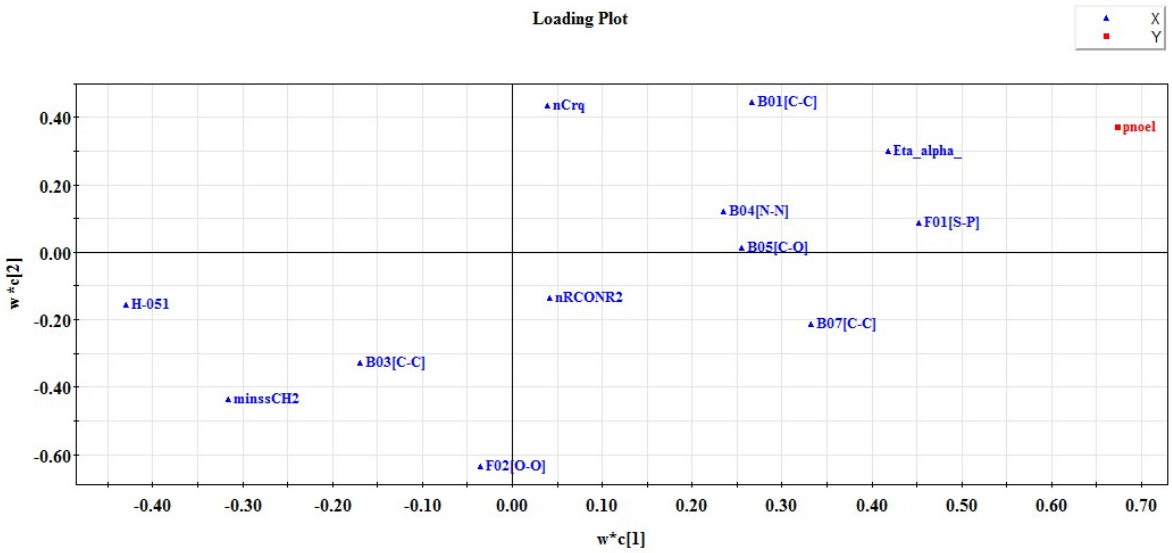

Fig.S14. Loading plot of Model IM4 (sub-chronic Toxicity; pNOEL endpoint)

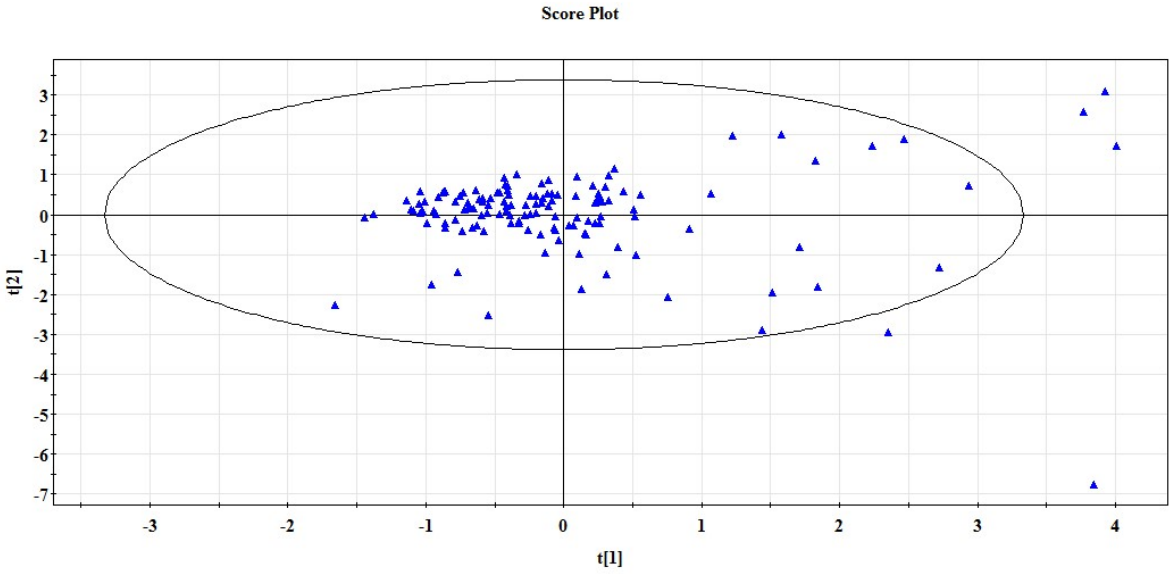

Fig.S15. Score plot of Model IM3 (sub-chronic Toxicity; pLOEL endpoint)

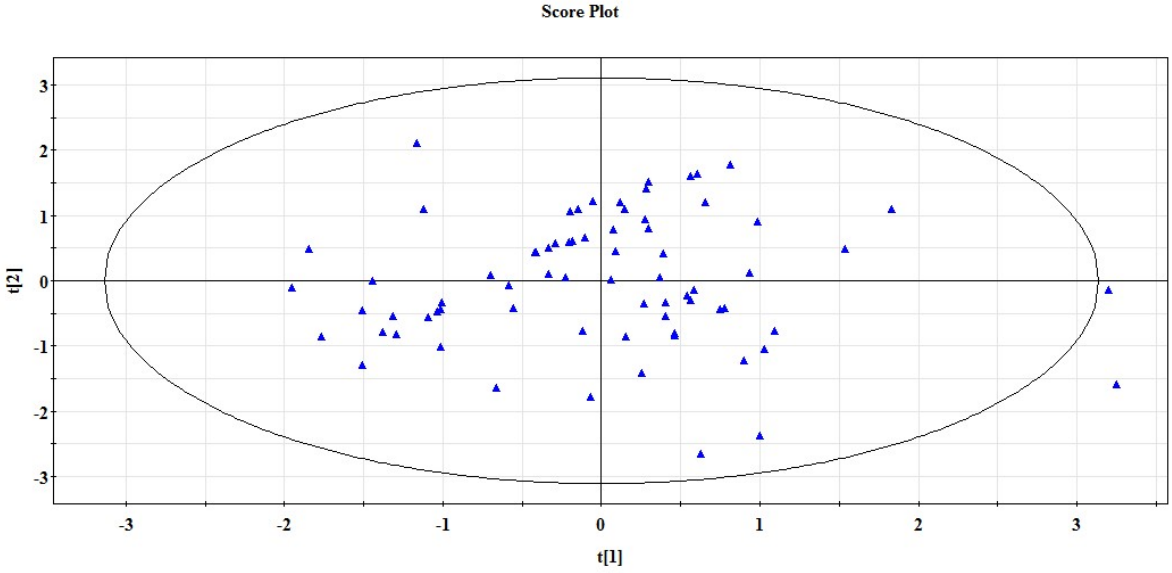

Fig.S16. Score plot of Model IM4 (sub-chronic Toxicity; pNOEL endpoint)

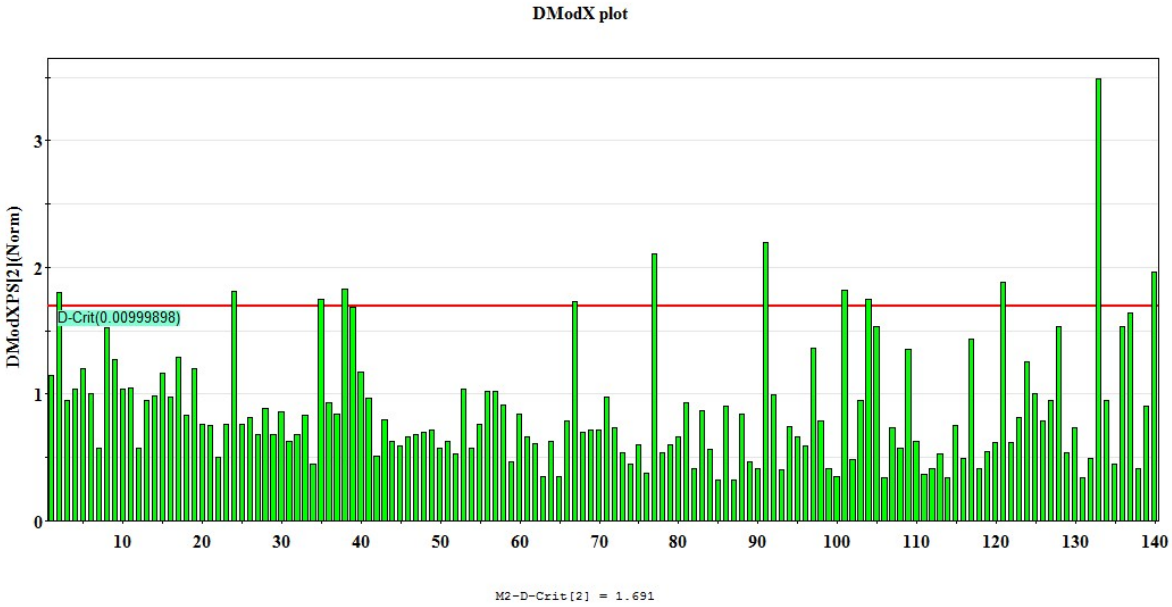

Fig.S17. DModX plot (training set) of Model IM1 (chronic Toxicity; pLOEL endpoint)

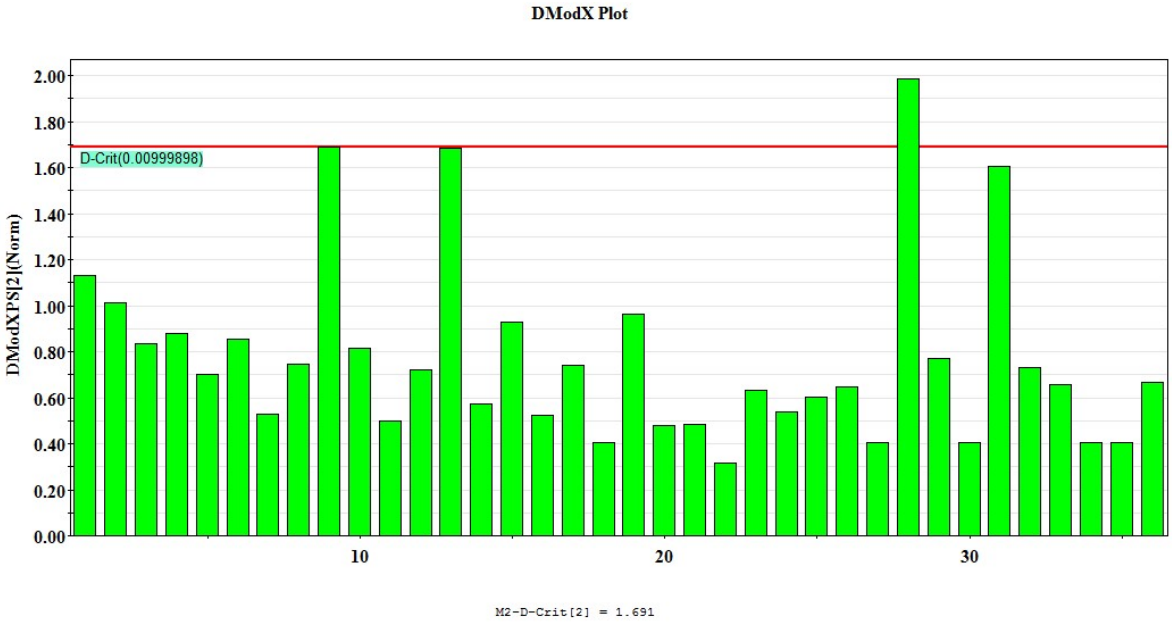

Fig.S18. DModX plot (test set) of Model IM1 (chronic Toxicity; pLOEL endpoint)

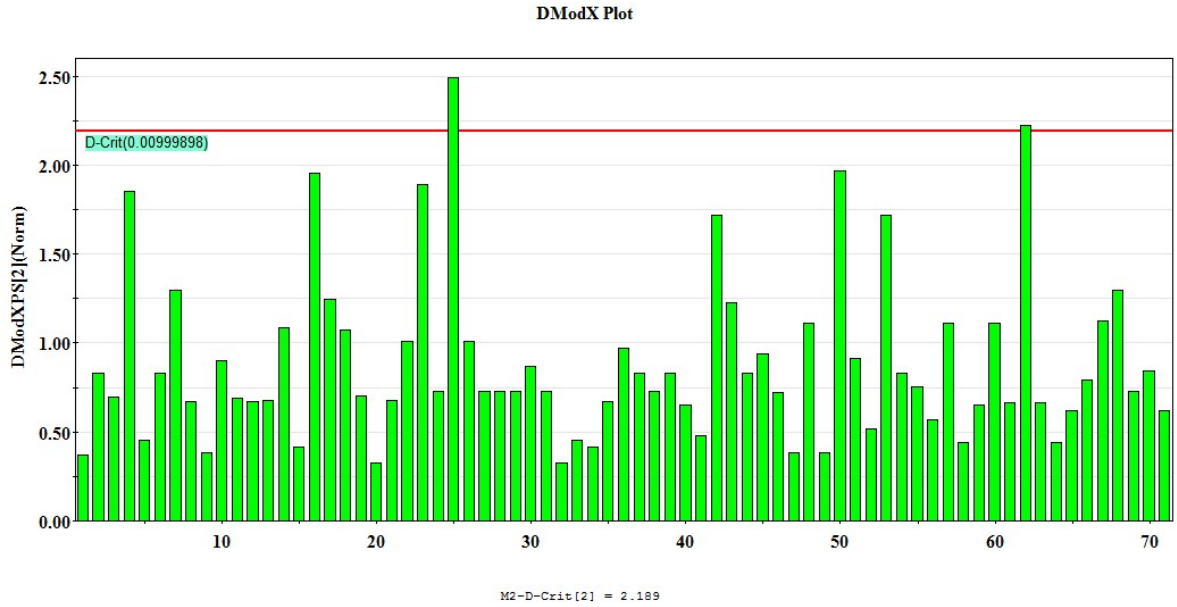

Fig.S19. DModX plot (training set) of Model IM2 (chronic Toxicity; pNOEL endpoint)

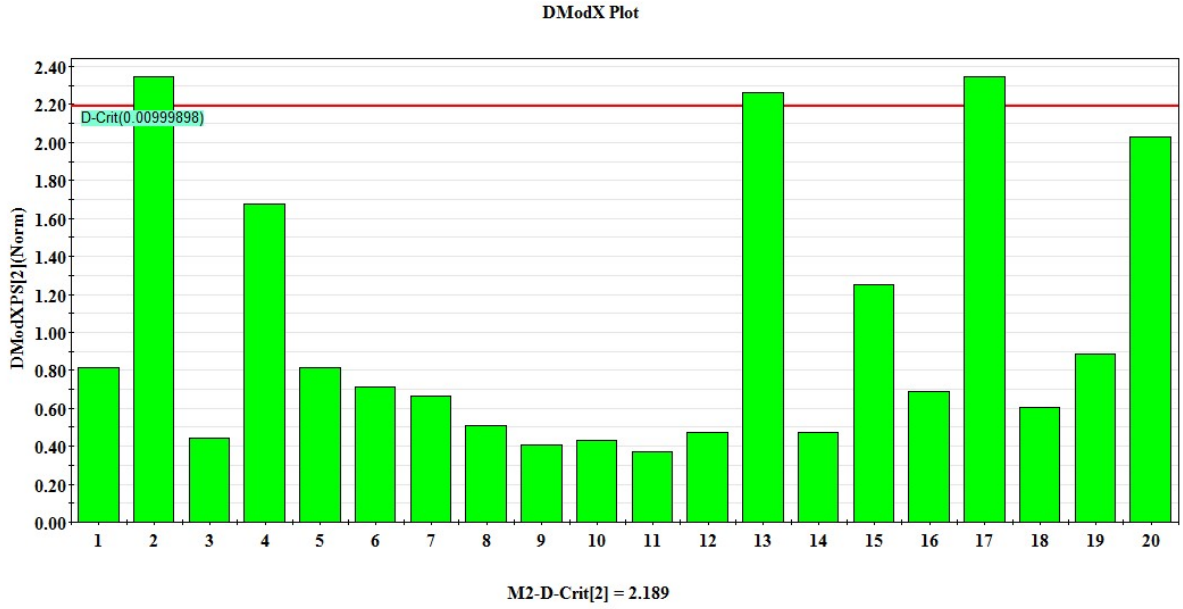

Fig.S20. DModX plot (test set) of Model IM2

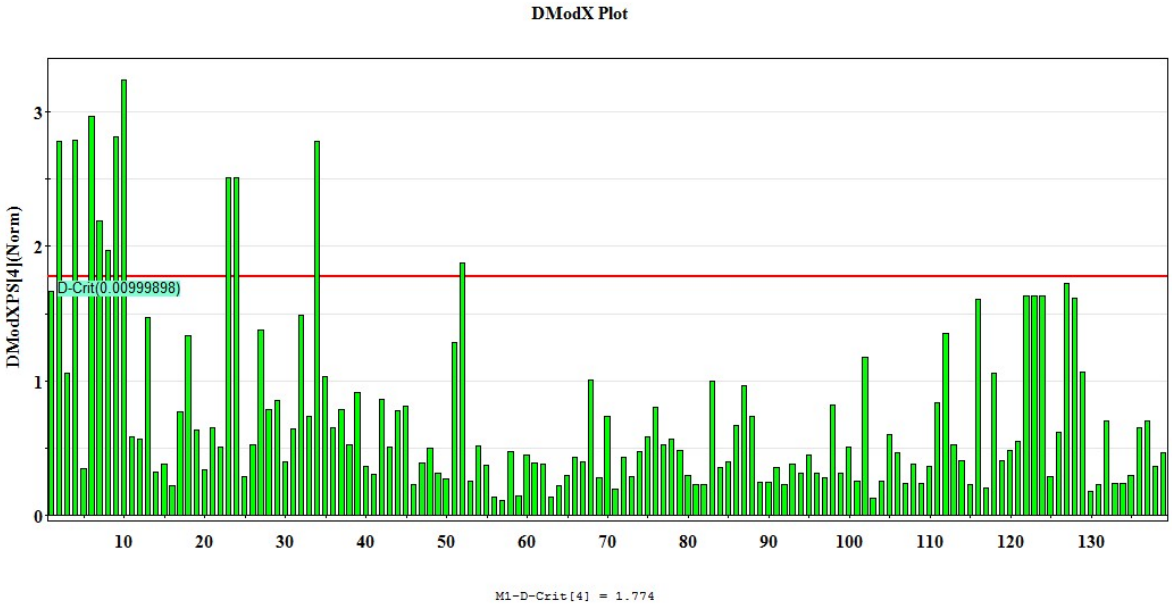

Fig.S21. DModX plot (training set) of Model IM3 (sub-chronic Toxicity; pLOEL endpoint)

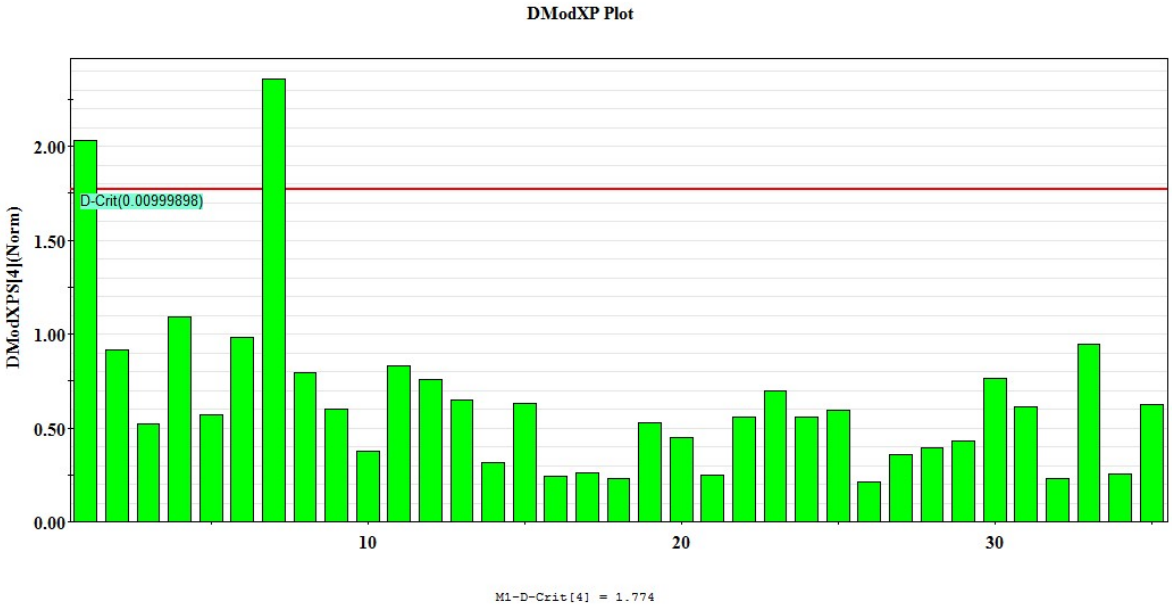

Fig.S22. DModX plot (test set) of Model IM3(sub-chronic Toxicity; pLOEL endpoint)

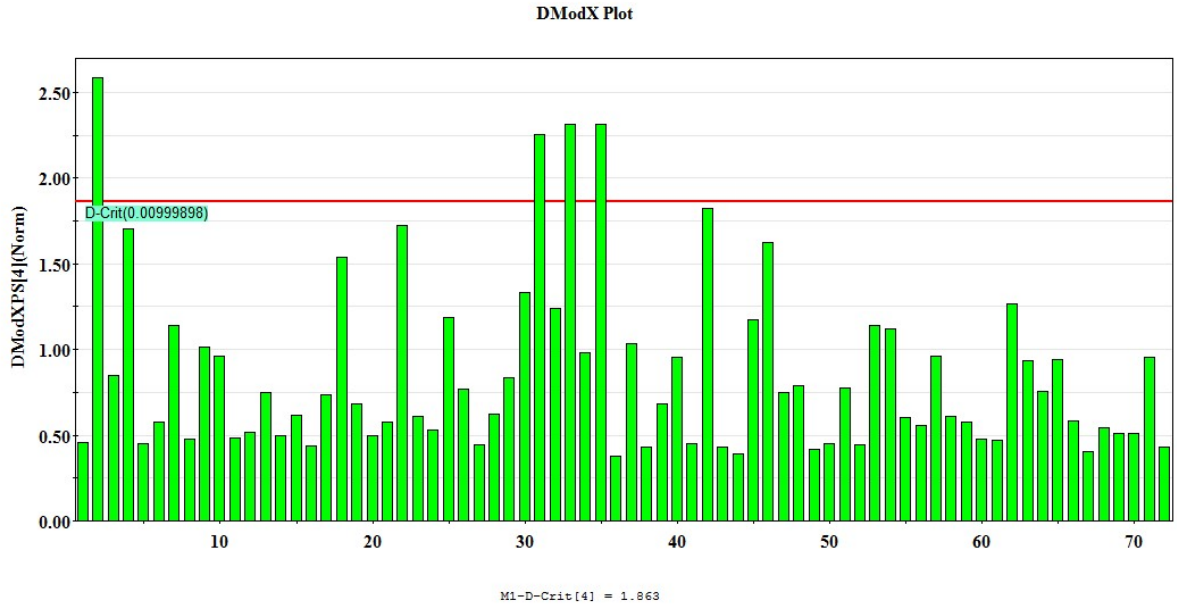

Fig.S23. DModX plot (training set) of Model IM4 (sub-chronic Toxicity; pNOEL endpoint)

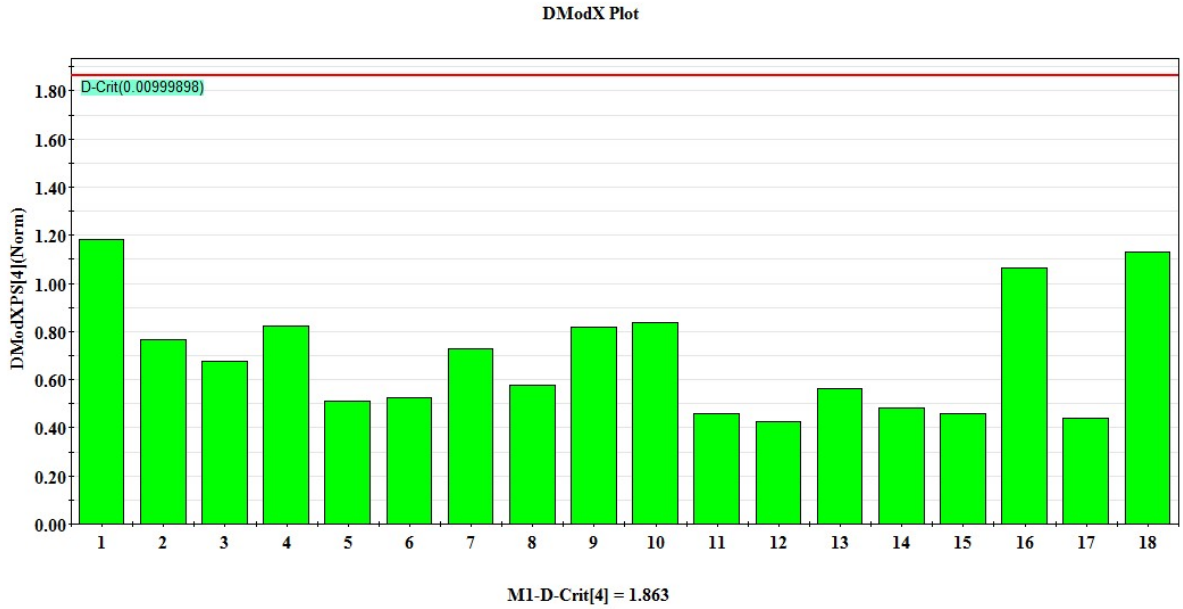

Fig.S24. DModX plot (test set) of Model IM4 (sub-chronic Toxicity; pNOEL endpoint)

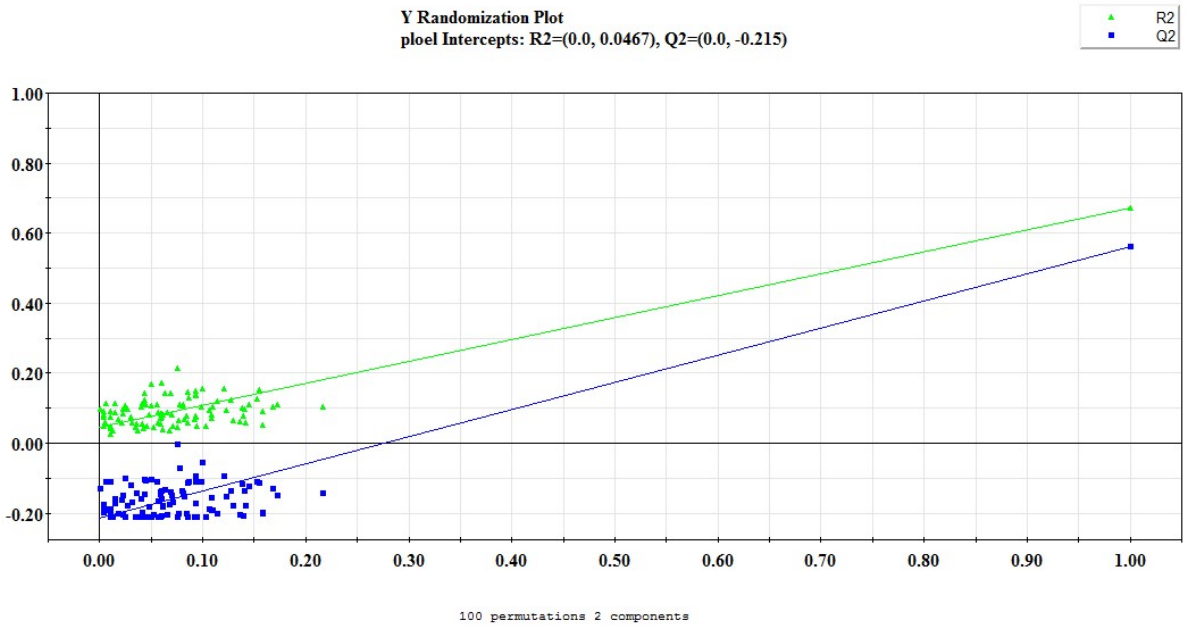

Fig.S25. Y Randomization plot of Model IM1 (chronic Toxicity; pLOEL endpoint)

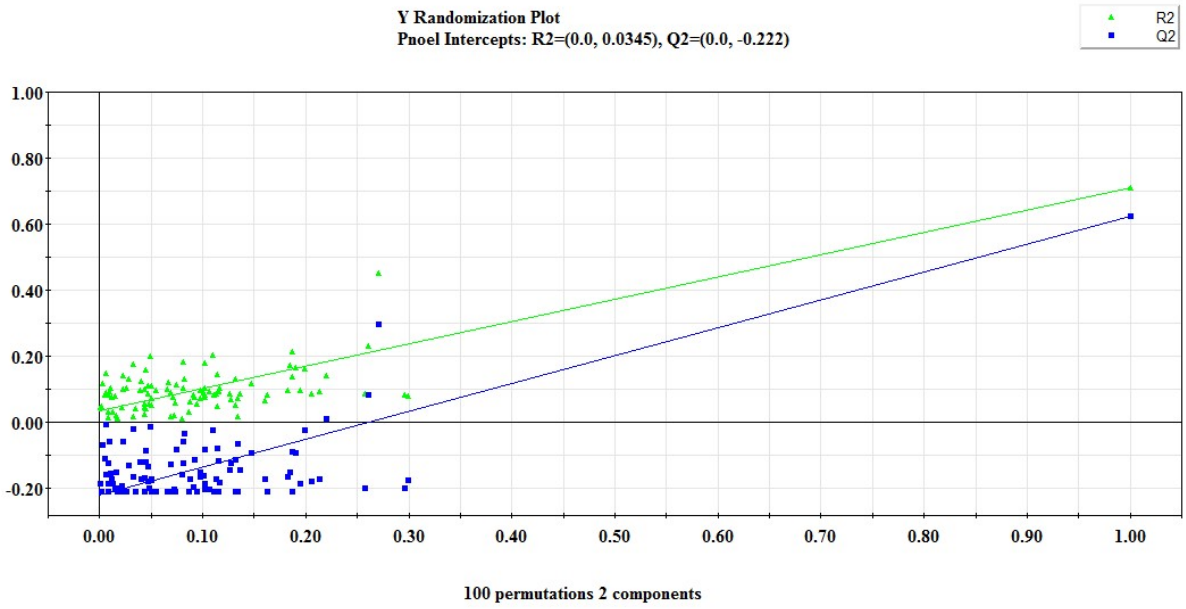

Fig.S26. Y Randomization plot of Model IM2 (chronic Toxicity; pNOEL endpoint)

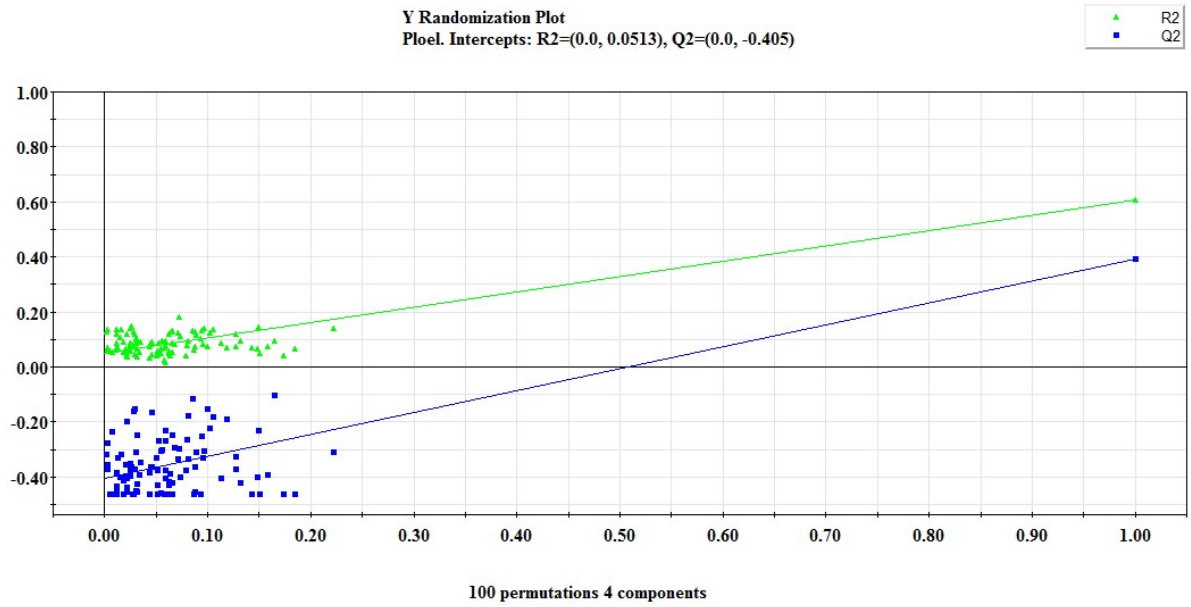

Fig.S27. Y Randomization plot of Model IM3 (sub-chronic Toxicity; pLOEL endpoint)

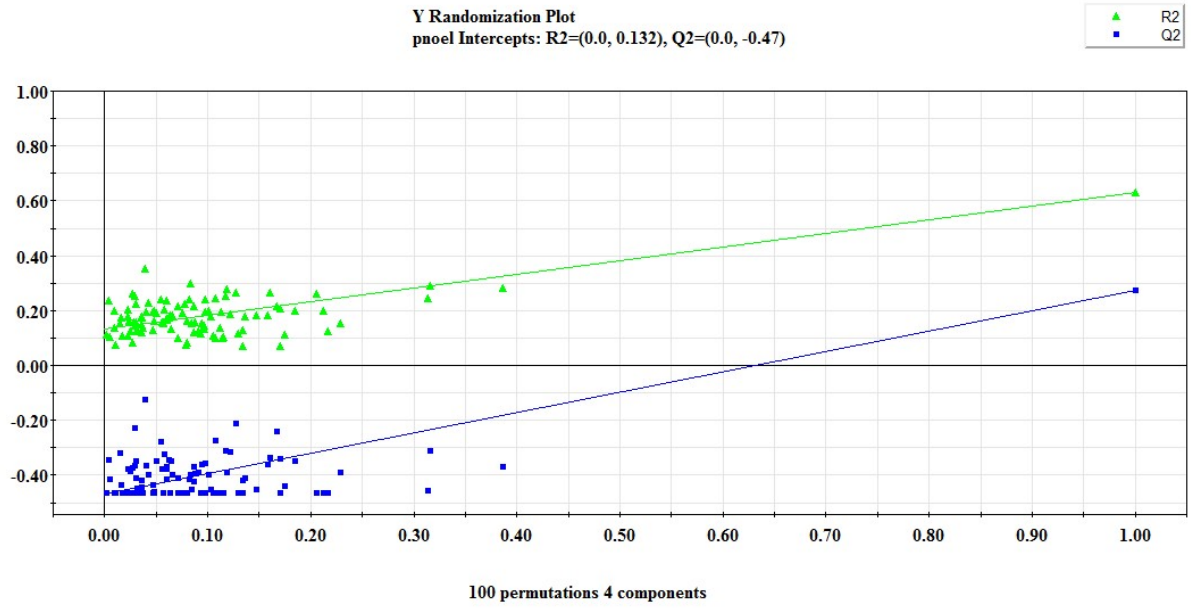

Fig.S28. Y Randomization plot of Model IM4 (sub-chronic Toxicity; pNOEL endpoint)

Table S1: Top 10 toxic pesticides predicted from our developed models

Top 10 toxic pesticides predicted from our developed models			
IM1: pLOEL chronic toxicity			
Compound	**Safety and Hazardous**	**Compound**	**Safety and hazardous**
Chlorpyrifos	Acute toxic and environmental hazards. High levels may result in severe sweating, loss of bowel control, severe muscle tremors, seizures, loss of consciousness, coma, or death [S1].	Chlorpyrifos-methyl	Irritant, environmental hazards. Neurotoxic effects have also been linked to poisoning with OP pesticides causing four neurotoxic effects in humans: cholinergic syndrome, intermediate syndrome, organophosphate-induced delayed polyneuropathy (OPIDP), and chronic organophosphate-induced neuropsychiatric disorder (COPIND). These syndromes result from acute and chronic exposure to OP pesticides [S2].
Chlorprazophos	Breathing or ingesting chlorpyrifos may result in a variety of nervous system effects, ranging from headaches, blurred vision, and salivation to seizures, coma, and death, depending on the amount and length of exposure [S3].	Chlorethoxyfos	Chronically toxic. Chlorethoxyfos is a cholinesterase or acetylcholinesterase (AChE) inhibitor. A cholinesterase inhibitor (or 'anticholinesterase') suppresses the action of acetylcholinesterase. Because of its essential function, chemicals that interfere with the action of acetylcholinesterase are potent neurotoxins, causing excessive salivation and eye-watering in low doses, followed by muscle spasms and ultimately death [S4].
Dialifos	Acute toxic, environmental hazards. Organophosphates & carbamates, acute poisoning [S5].	Fenmezoditiaz	Threshold of Toxicological Concern (Cramer Class): High (class III) [S6].
Anilofos	Irritant, Organophosphorus herbicides, Acute Tox. 4 (100%)	Isoxathion	Acute toxic, environmental hazards. Other Poison – Organophosphate [S8]

	[S7].		
Pyraclofos	Acute toxic, signal-danger [S9].	Kelevan	Acute toxic, environmental hazards. Hazardous to the aquatic environment (chronic) - category 2 [S10].
IM2: pNOEL chronic toxicity			
Etrimfos	Irritant, environmental hazards. Other Poison – Organophosphate [S11].	Chlorphoxim	Acute toxic [S12].
Amidothioate	Organophosphate insecticide. Threshold of Toxicological Concern (Cramer Class): High (class III) [S13].	Chlorprazophos	Breathing or ingesting chlorpyrifos may result in a variety of nervous system effects, ranging from headaches, blurred vision, and salivation to seizures, coma, and death, depending on the amount and length of exposure [S3].
Phosacetim	Organophosphates & carbamates, acute poisoning [S14]	Chlorthion	Irritant and environmental hazards. Organophosphates & carbamates, acute poisoning [S15]
Propetamphos	Acute and environmental hazards. Other Poison – Organophosphate [S16].	Isazofos	Acute toxic, environmental, and health hazards. Other Poison – Organophosphate [S17].
Azothoate	Irritant, Acute toxicity - category 4 [S18].	Menazon	Irritant, Other Poison – Organophosphate [S19].
IM3: pLOEL sub-chronic toxicity			
Camphechlor	Camphechlor causes liver tumors in mice and thyroid tumors in rats and	Dieldrin	Acute toxic, health, and environmental hazards. Cancer Classification: Group B2 Probable Human Carcinogen [S21]

	is classified by the IARC as a possible human carcinogen (group 2B) [S20].		
Merphos	Irritant. Neurotoxin - Predominantly motor Other Poison – Organophosphate [S22]	Endrin	Acute toxic, environmental hazards. Endrin poisoning affects primarily the nervous system. Exposure causes various harmful effects including hyperexcitability, severe central nervous system damage, and death. Endrin is also believed to cause birth defects [S23].
Lime sulphur	Occupational hepatotoxin - Secondary hepatotoxins: the potential for toxic effects in the occupational setting is based on cases of poisoning by human ingestion or animal experimentation [S24].	Copper II chloride	Acute toxic, environmental hazards. Very-high doses of copper can cause damage to your liver and kidneys, and can even cause death. Copper may induce allergic responses in sensitive individuals [S25].
Methiotepa	Myelosuppression [S26]	Tetcyclacis	Acute toxic [S27].
Cadusafos	Acute toxic and environmental hazards. Other Poison - Organophosphate [S28].	Chlorphonium	Acute toxic [S29].
IM4: pNOEL sub-chronic toxicity			

Flupoxam	Environmental hazards [S30]	Phosmet	Acute toxic, health and environmental hazards [S31].
Ethoprophos	Acute and environmental hazards. Cancer Classification: Likely to be Carcinogenic to Humans [S32].	Triflusulfuron	Chronic and long-term toxic effects [S33].
Trifloxysulfuron	Expected chronic toxicity [S34].	Triflusulfuron-methyl	Health and environmental hazards Hazardous to the aquatic environment (chronic) - category 1 [S35].
Dialifos	Acute toxic, environmental hazards. Organophosphates & carbamates, acute poisoning [S5].	Amidithion	Irritant, acute toxic [S36].
Mecarphon	Chronic effects [S37].	Lythidathion	Acute toxic, dangerous organophosphate substance. Short and long-term health effects [S38-39].

References:

S1. https://pubchem.ncbi.nlm.nih.gov/compound/2730

S2. https://pubchem.ncbi.nlm.nih.gov/compound/21803

S3.https://wwwn.cdc.gov/TSP/ToxFAQs/ToxFAQsDetails.aspx?faqid=494&toxid=88#:~:text=Highlights,amount%20and%20length%20of%20exposure.

S4. https://pubchem.ncbi.nlm.nih.gov/compound/91655

S5. https://pubchem.ncbi.nlm.nih.gov/compound/25146

S6. http://sitem.herts.ac.uk/aeru/ppdb/en/Reports/3363.htm#none

S7. https://pubchem.ncbi.nlm.nih.gov/compound/91687

S8. https://pubchem.ncbi.nlm.nih.gov/compound/29307

S9. https://pubchem.ncbi.nlm.nih.gov/compound/93460

S10. https://pubchem.ncbi.nlm.nih.gov/compound/20226

S.11 https://pubchem.ncbi.nlm.nih.gov/compound/37995

S.12 https://pubchem.ncbi.nlm.nih.gov/compound/5360461

S13. http://sitem.herts.ac.uk/aeru/ppdb/en/Reports/2702.htm

S14. https://pubchem.ncbi.nlm.nih.gov/compound/9570168

S15. https://pubchem.ncbi.nlm.nih.gov/compound/10372

S16. https://pubchem.ncbi.nlm.nih.gov/compound/5372405

S17. https://pubchem.ncbi.nlm.nih.gov/compound/39223

S18. https://pubchem.ncbi.nlm.nih.gov/compound/79914

S19. https://pubchem.ncbi.nlm.nih.gov/compound/6543

S20. https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/toxaphene

S21. https://pubchem.ncbi.nlm.nih.gov/compound/969491

S22. https://pubchem.ncbi.nlm.nih.gov/compound/9011

S23. https://pubchem.ncbi.nlm.nih.gov/compound/3048

S24. https://pubchem.ncbi.nlm.nih.gov/compound/121494065

S25. https://pubchem.ncbi.nlm.nih.gov/compound/11969527

S26. https://go.drugbank.com/drugs/DB04572

S27. https://pubchem.ncbi.nlm.nih.gov/compound/92396

S.28 https://pubchem.ncbi.nlm.nih.gov/compound/91752

S29. https://pubchem.ncbi.nlm.nih.gov/compound/8286

S30. https://pubchem.ncbi.nlm.nih.gov/compound/86353

S31. https://pubchem.ncbi.nlm.nih.gov/compound/12901

S32.https://pubchem.ncbi.nlm.nih.gov/compound/3289

S33. https://www3.epa.gov/pesticides/chem_search/hhbp/R038432.pdf

S34. https://www.apvma.gov.au/sites/default/files/publication/14086-prs-trifloxysulfuron.pdf

S35. https://pubchem.ncbi.nlm.nih.gov/compound/92434

S36. https://pubchem.ncbi.nlm.nih.gov/compound/13525

S37. https://pubmed.ncbi.nlm.nih.gov/7344408/

S38. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6786676.

S39. https://pubmed.ncbi.nlm.nih.gov/1516789/