able 3. Selected mechanisms of acute toxicity.[1]

MIE or upstream key event	Example stressor	Relevant AOP
GABA receptor inhibition	Fipronil	Binding to the picrotoxin site of ionotropic GABA receptors leading to epileptic seizures[a]
Sodium channel inhibition	Pyrethroids	Axonal sodium channel modulation leading to acute mortality[b]
Protein synthesis inhibition	Ricin	
Sodium-potassium ATPase inhibition	Digoxin	
Mitochondrial inhibition	2-Buten-1-ol, 1-thenyl-4,4,4-trifluoro-3-trifluoromethyl-	
Binding of benzodiazepine sites on GABA receptor	Tetrazepam	
Acetylcholinesterase inhibition	4-(Methylamino)-3,5-xylyl methylcarbamate	Acetylcholinesterase inhibition leading to acute mortality[c]
GSH depletion followed by covalent binding of reactive metabolite to cellular proteins	Acetaminophen	
Michael acceptor reaction	Acrolein	
Voltage-gated sodium channel inhibition	Sodium valproate	
NMDA receptor antagonism	Methadone	
Anticoagulation	Coumadin	
Dopaminergic D2 receptor antagonism	Thioridazine hydrochloride	

1 This table provides an outline of the some of the known mechanisms involved in acute systemic toxicity along with prototypical initiators. In some cases, the exact molecular initiating event (MIE) isn't known. Examples of adverse outcome pathways (AOPs) under development in the OECD AOP Wiki are noted and can be found on the web: a) https://aopwiki.org/wiki/index.php/Aop:10 b) https://aopwiki.org/wiki/index.php/Aop:96; c) https://aopwiki.org/wiki/index.php/Aop:16.