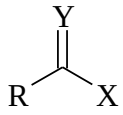
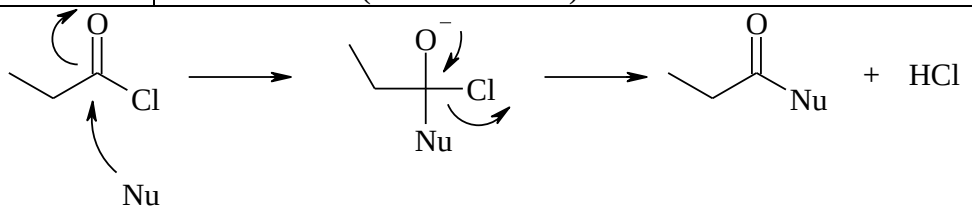
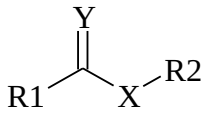
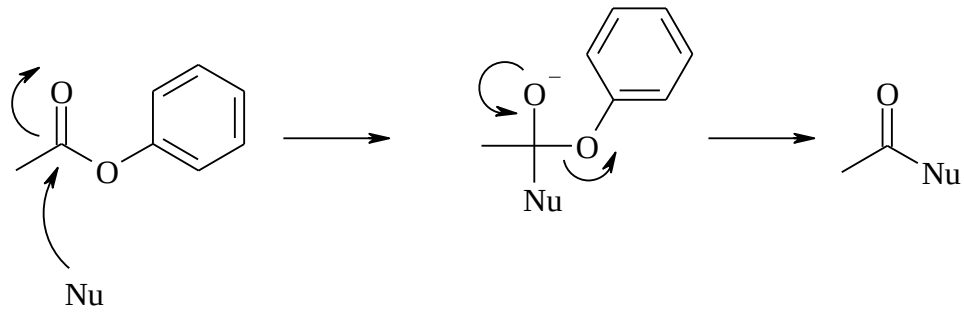
About section of a profiler
Name of the profiler
Protein binding by OECD
Developer; Donator; date; version
Developer: School of Pharmacy and Chemistry, Liverpool John Moores University, UK ***Donator:*** European Chemicals Agency (ECHA); Organization for Economic Co-operation and Development (OECD) ***Version:*** 2.3 December 2016
Relevance/Applicability to endpoint(s)
This profiler is intended to be used for the assessment of endpoints in which covalent binding to a protein has been shown to be the molecular initiating event for low molecular weight chemicals. The profiler has been developed from mechanistic knowledge of the electrophilic chemistry of covalent protein binding for direct acting electrophiles only – importantly it has been developed from a systematic review of the literature and not from the analysis of a single toxicological dataset.
Relevance/Applicability to particular chemical classes
This profiler is applicable only to organic chemicals that have a molecular weight less than 1000 g/mol. It is applicable only to the chemical classes for which it contains structural alerts; the absence of a structural alert should not be taken as an absence of toxicity. This profiler contains structural alerts for direct acting electrophiles only – oxidation and/or metabolism are not accounted for (appropriate Toolbox simulators should be applied, if required).
Approach used to develop the profiler - Concise but informative description of:
a) The aim of the profiler was to identify structural alerts associated with organic, low molecular weight chemicals capable of forming covalent bonds with a protein. The structural alerts were derived from knowledge of the molecular initiating event - covalently binding to a protein. It was developed from a systematic review of the literature, rather than from the analysis of a single toxicological dataset.
b) The profiler was developed from a mechanistic rationale that the molecular initiating event for covalent bond formation with proteins. Importantly, this was achieved by reviewing the literature relating to the chemistry, rather than an analysis of toxicological datasets.
c) The profiler was developed from an extensive review of the literature relating to the chemistry of covalent bond formation with a protein. A full list of the literature included can be found in the reference listed in section d.
d) An overview of the mechanistic chemistry and underlying principles of the structural alerts within this profiler can be found in: Enoch et al (2010) *A review of the electrophilic reaction chemistry involved in covalent protein binding.* Critical Reviews in Toxicology, 41, p783-802
Summary description of profiles/alerts within the profiler
It is not possible to provide metrics relating to this profiler as it was not developed from an analysis of toxicological datasets. It was developed from an extensive review of the chemistry related to the formation of a covalent bond between a low molecular weight chemical and a protein.
Similar to other profilers
A number of related endpoint specific profilers exist in the OECD QSAR Toolbox relating to

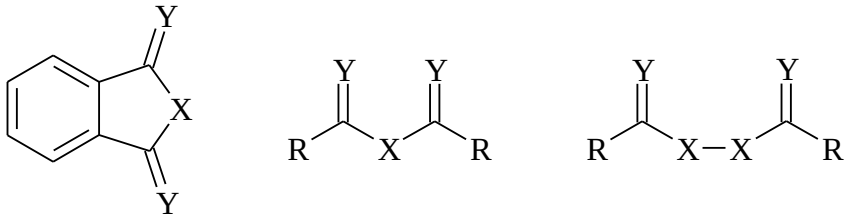
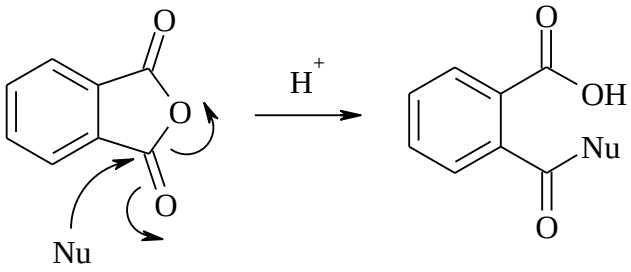
genotoxicity. The protein binding by OECD profiler should be used first, with endpoint specific profilers (which have been developed from an analysis of toxicological data) being used to sub-categorise, where possible. This profiler contains structural alerts for direct acting electrophiles only – oxidation and/or metabolism are not accounted for (appropriate Toolbox simulators should be applied, if required).
Short description of update version
SMARTS language for describing molecular patterns, i.e. structural boundaries, structural alerts has been implemented in OECD QSAR Toolbox 4.0. As a result ***Protein binding by OECD*** has been rewritten but without modifying the knowledge and/or the logic it is based on. Only small distinctions are expected in the profiling results between Toolbox v.3.4 and v 4.0 due to different interpretation of the molecular structures, e.g. for heterocyclic/heteroaromatic compounds. Further general modifications are associated with the new 2D editor which allows the structural boundaries to be coded more accurately according to the descriptions of the categories. Examples for categories with possible discrepancies between TB 3.4 and TB 4.0: Acetates; Allyl acetates and related chemicals.
Disclaimer
The structural boundaries used to define the chemical classes (e.g. "Alcohol" – chemical class from "Organic functional group" profiler) or alerting groups responsible for the binding with biological macromolecules (e.g. "Aldehydes" – structural alert for protein binding), represent structural functionalities in the molecule which could be used for building chemical categories for subsequent data gap filling. They are not recommended to be used directly for prediction purposes (as SARs).

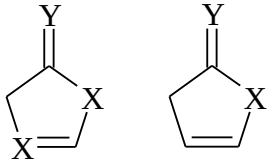
Individual profile/alert	
Name	Acyl halides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, nitrogen X (leaving group) = halogen, azide Y = oxygen, sulphur
Mechanism	An acylation mechanism involving nucleophilic attack at the carbonyl (or sulfinyl) has been suggested as being responsible for the activity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used	An extensive review of the literature was performed enabling the

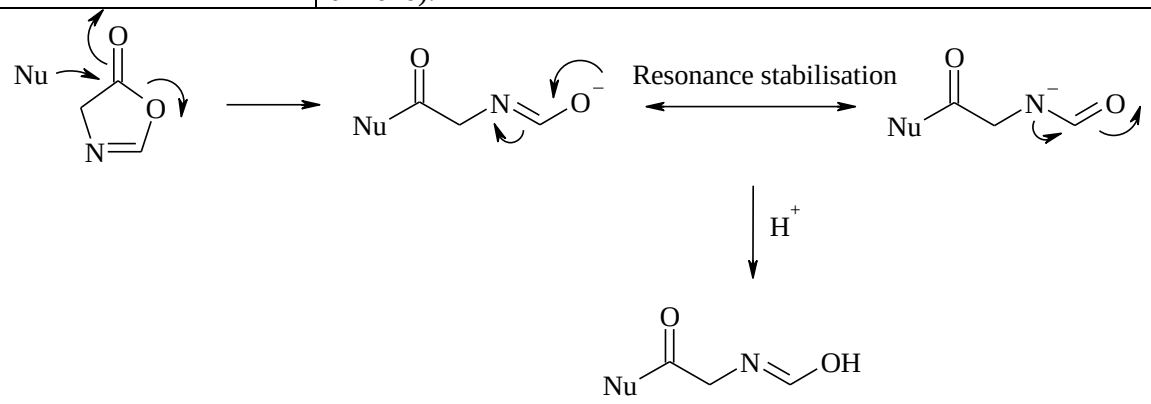
for profile development	chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

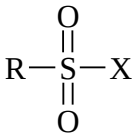
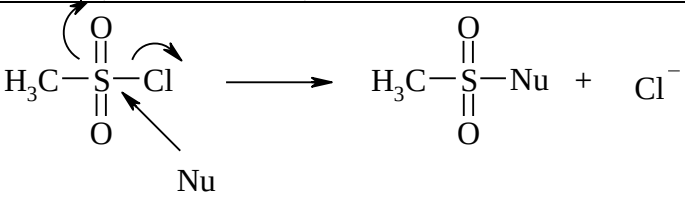
Individual profile/alert	
Name	Acetates
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = aromatic, heteroaromatic, heterocyclic, alkene, alkyne R1 and R2 can be part of a ring e.g. dihydro-courmarin. Y = oxygen or sulphur X = oxygen (acetates), sulphur (thioacetates), nitrogen (acetanilides)
Mechanism	An acylation mechanism has been suggested for chemicals of this type (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert

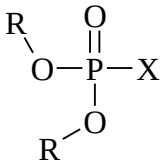
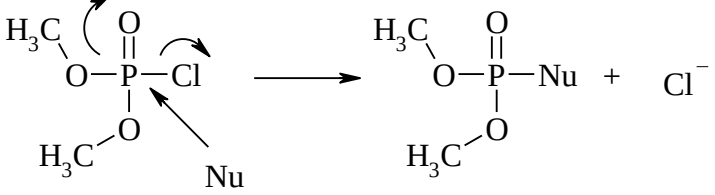
Name	Anhydrides
Type of profile	Structural alert
Description/applicability domain	 X = oxygen, sulphur Y = oxygen (carbonyl), sulphur (sulfinyl) R = any carbon or hydrogen
Mechanism	An acylation mechanism has been suggested for chemicals of this type (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Azlactones
Type of profile	Structural alert
Description/applicability domain	 Y = oxygen (carbonyl), sulphur (sulfinyl) X = oxygen, sulphur, nitrogen
Mechanism	An acylation mechanism has been suggested for chemicals of this type. Importantly, these chemicals are only active due to the ability of the unsaturated moiety to stabilise the leaving group anion (the

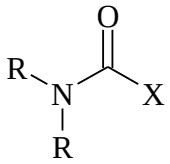
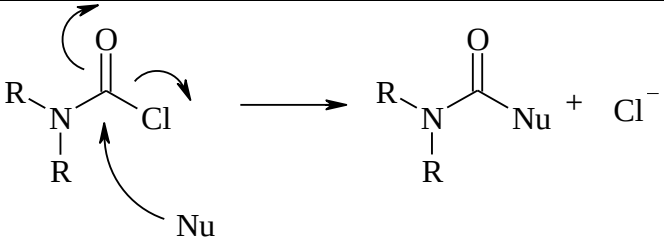
	equivalent γ-lactone-type structures are not protein reactive) (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

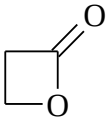
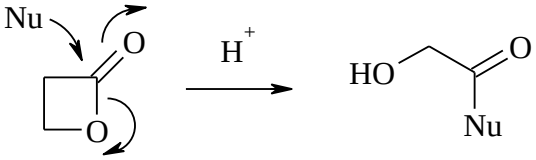
Individual profile/alert	
Name	Sulphonyl halides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen X = halogen, cyano
Mechanism	An acylation mechanism involving attack at the sulphur has been suggested for the protein binding potential of this class of chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define

	the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

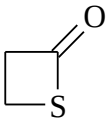
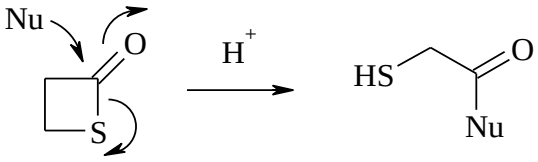
Individual profile/alert	
Name	Phosphonic acid halides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An acylation mechanism has been suggested a being responsible for the protein binding ability of this class of chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Dialkyl carbamoylhalides
Type of profile	Structural alert

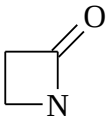
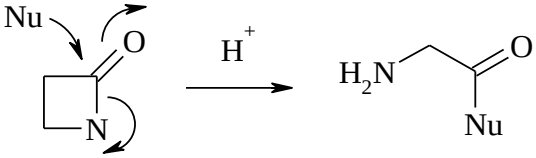
Description/applicability domain	 X = halogen R = any carbon
Mechanism	An acylation mechanism has been suggested a being responsible for the protein binding ability of this class of chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

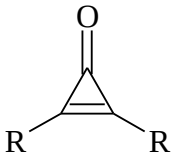
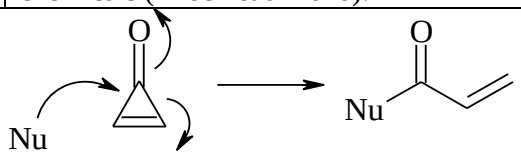
Individual profile/alert	
Name	β-Lactones
Type of profile	Structural alert
Description/applicability domain	
Mechanism	An acylation mechanism involving a ring opening reaction has been suggested to be responsible for the protein binding ability of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein

	binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

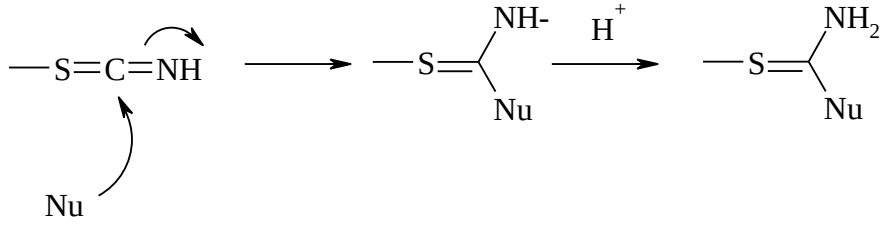
Individual profile/alert	
Name	Thio-lactones
Type of profile	Structural alert
Description/applicability domain	
Mechanism	An acylation mechanism involving a ring opening reaction has been suggested to be responsible for the protein binding ability of these chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	α-Lactams
Type of profile	Structural alert

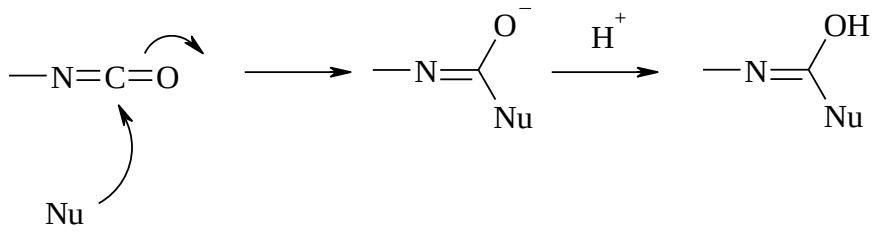
Description/applicability domain	
Mechanism	An acylation mechanism involving a ring opening reaction has been suggested to be responsible for the protein binding ability of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

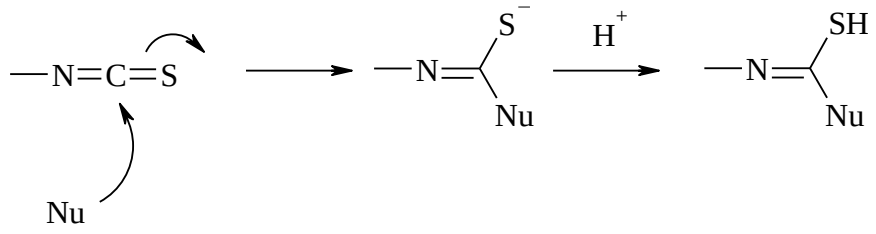
Individual profile/alert	
Name	Cyclopropenones
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	An acylation mechanism involving a ring opening reaction has been suggested to be responsible for the protein binding ability of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined

	and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

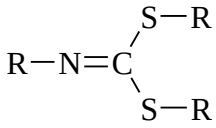
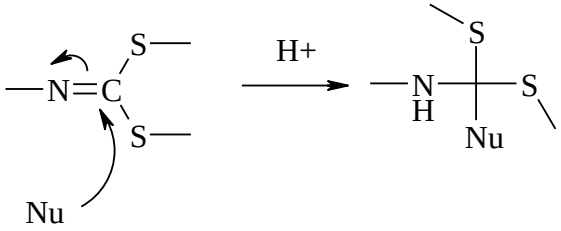
Individual profile/alert	
Name	Thiocyanates
Type of profile	Structural alert
Description/applicability domain	R—S=C=NH R = any carbon
Mechanism	An acylation mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

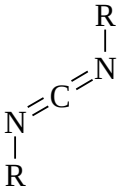
Individual profile/alert	
Name	Isocyanates
Type of profile	Structural alert
Description/applicability domain	R—N=C=O R = any carbon
Mechanism	An acylation mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

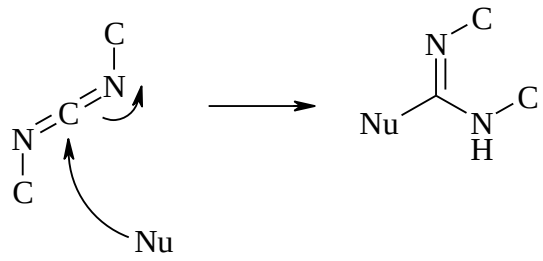
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

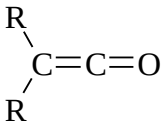
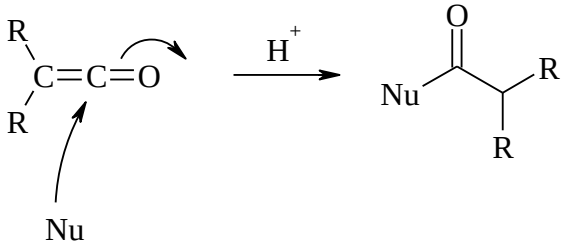
Individual profile/alert	
Name	Isothiocyanates
Type of profile	Structural alert
Description/applicability domain	R—N=C=S R = any carbon
Mechanism	An acylation mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.

profilers)	
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

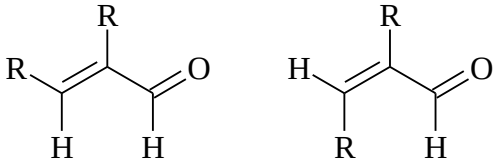
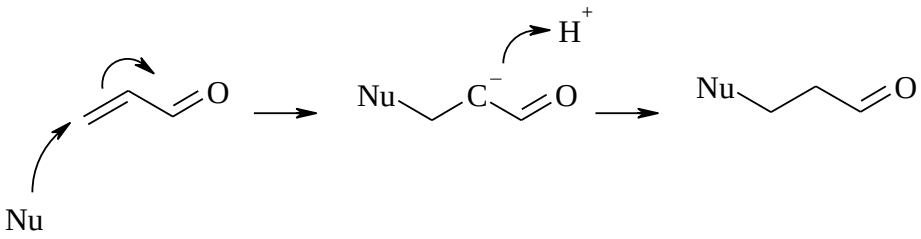
Individual profile/alert	
Name	Dithiocarbonimidic acid esters
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An acylation mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

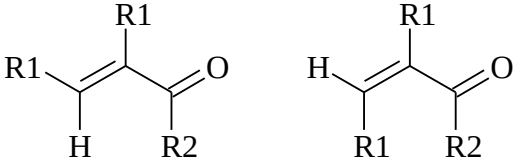
Individual profile/alert	
Name	Carbodiimides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An acylation mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

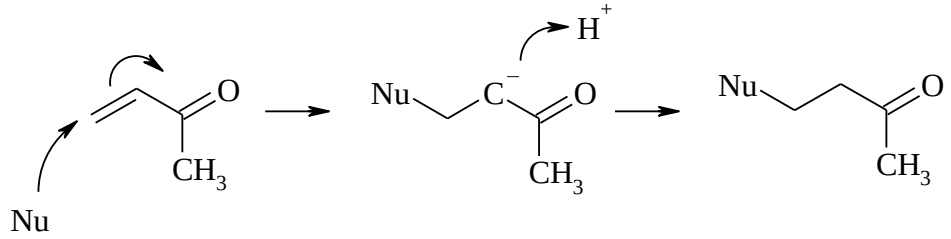
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

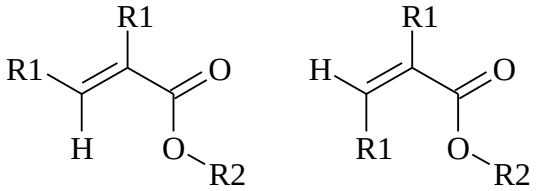
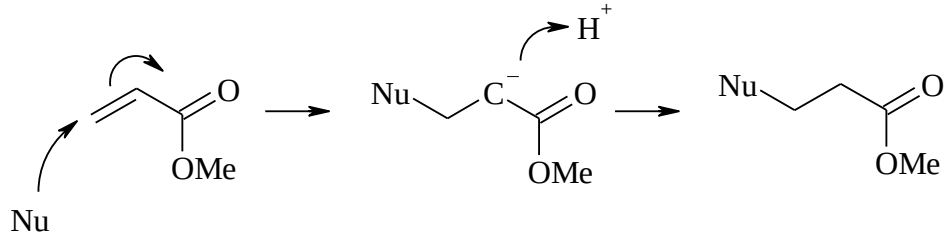
Individual profile/alert	
Name	Ketenes
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	An acylation mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the	N/A – all alerts in this profiler were developed from a review of the

profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

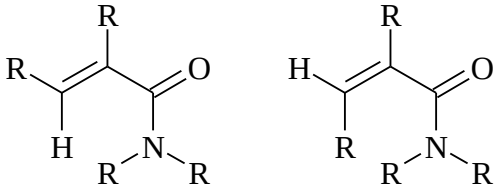
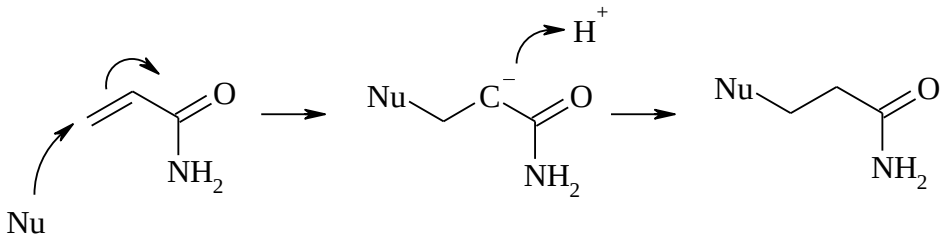
Individual profile/alert	
Name	Polarised alkene - aldehydes
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkene - ketones
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen

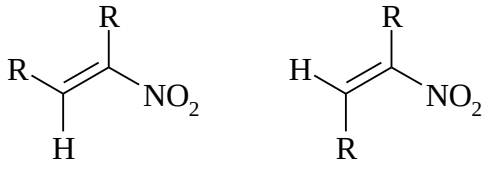
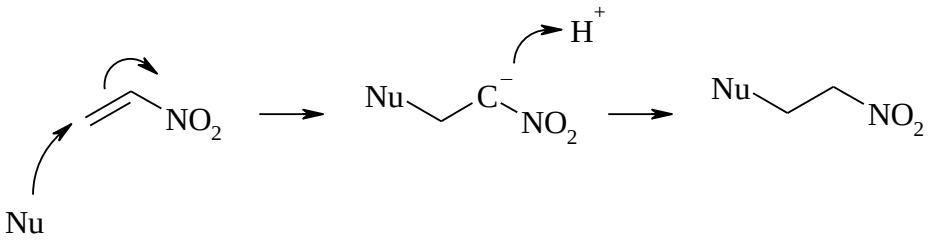
	R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

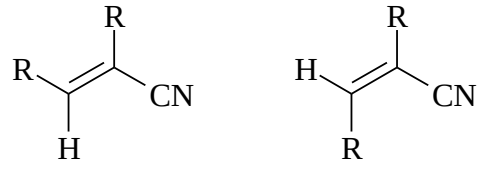
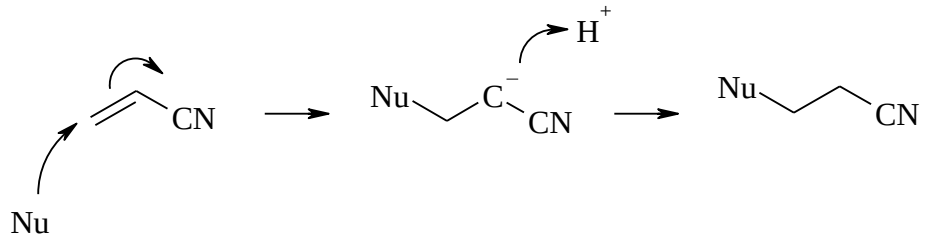
Individual profile/alert	
Name	Polarised alkene - esters
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the

	molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

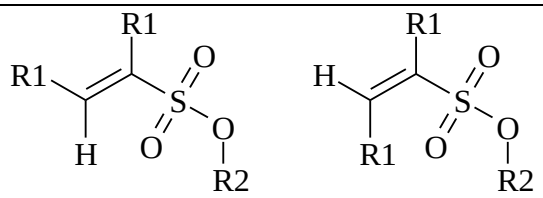
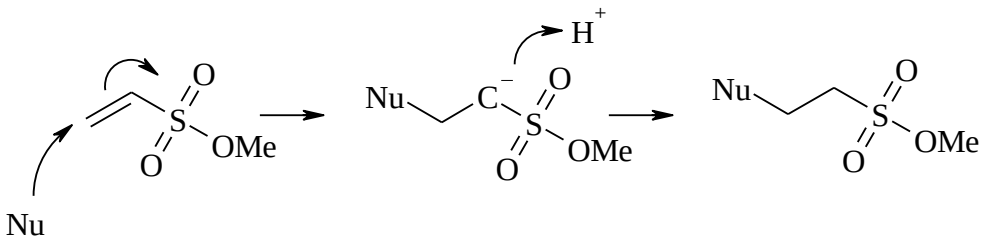
Individual profile/alert	
Name	Polarised alkene - amides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

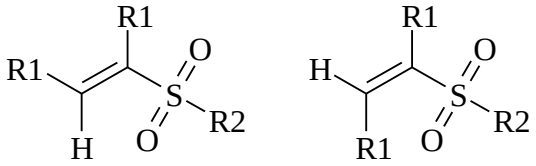
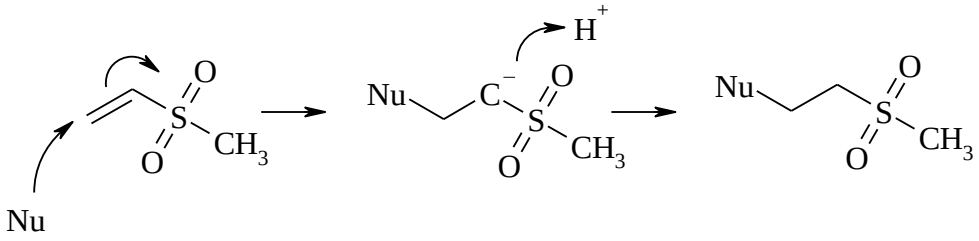
Individual profile/alert	
Name	Polarised alkene - nitros
Type of profile	Structural alert

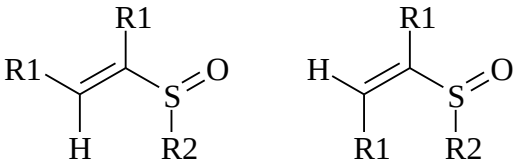
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

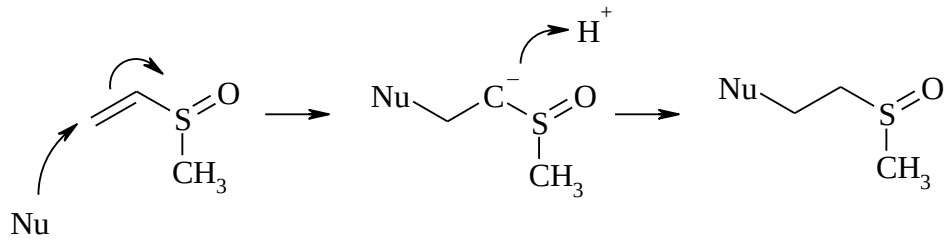
Individual profile/alert	
Name	Polarised alkene - cyanos
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for	N/A – all structural alerts in this profiler were developed from a

profile development	review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

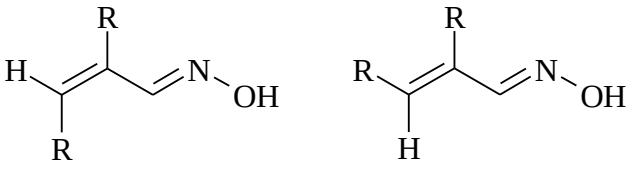
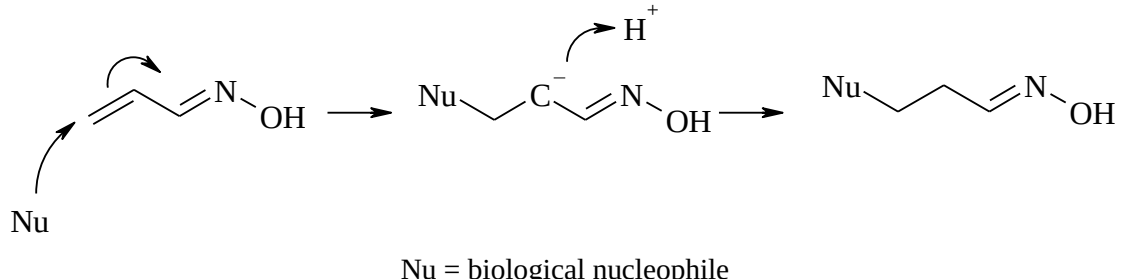
Individual profile/alert	
Name	Polarised alkene - sulfonates
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkene - sulfones
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

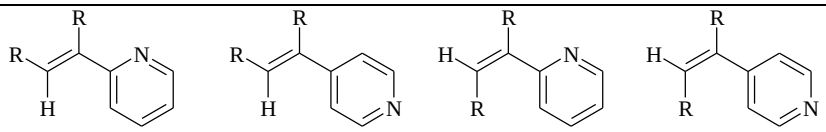
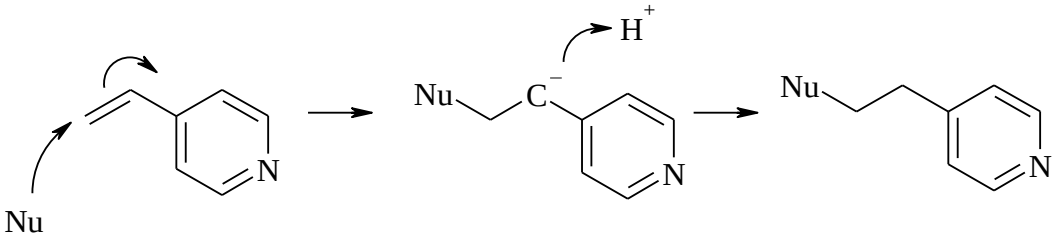
Individual profile/alert	
Name	Polarised alkene - sulfinyls
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

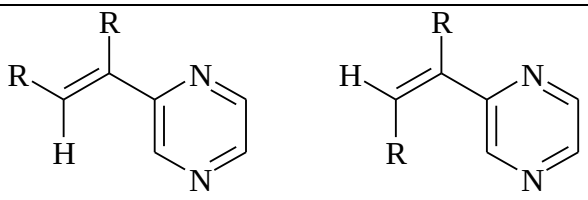


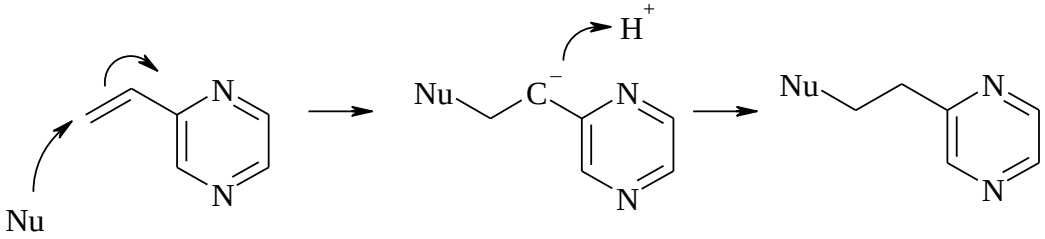
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

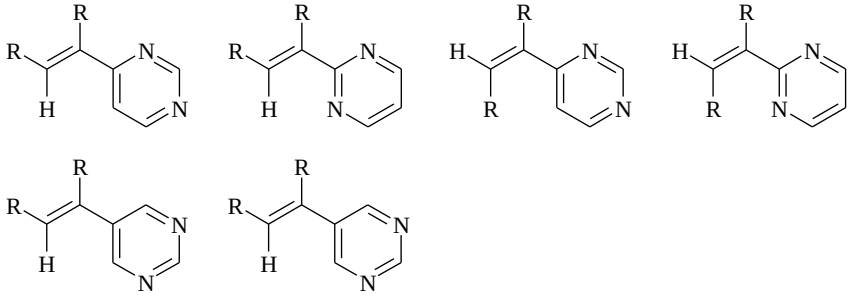
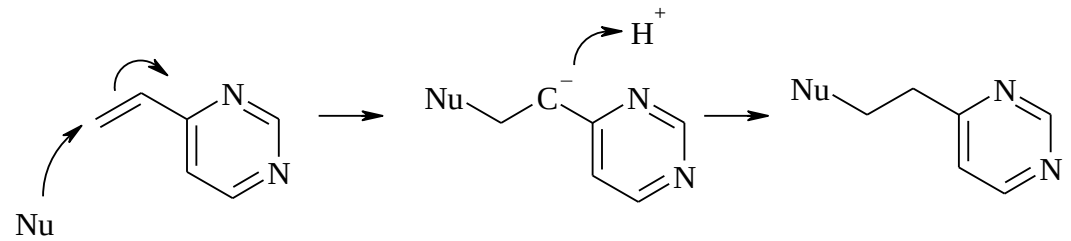
Individual profile/alert	
Name	Polarised alkene - oximes
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.

Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

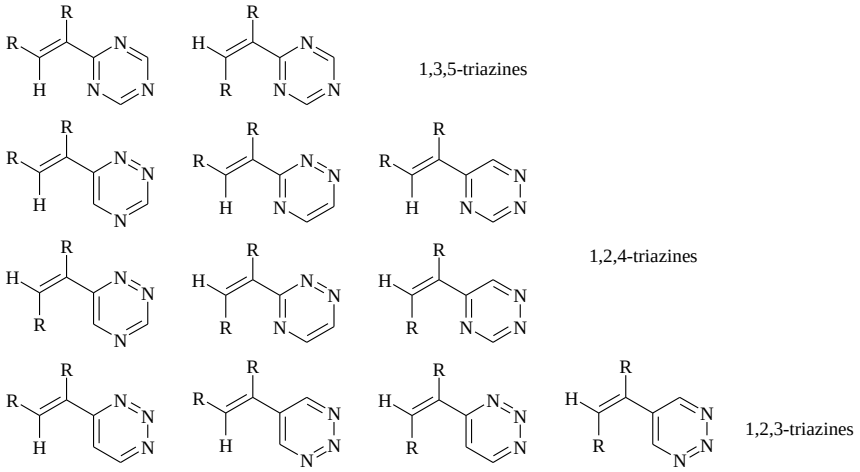
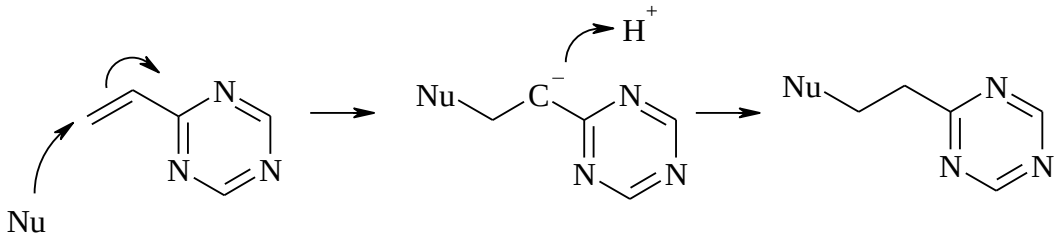
Individual profile/alert	
Name	Polarised alkene - pyridines
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkene - pyrazines
Type of profile	Structural alert
Description/applicability domain	

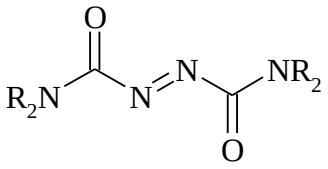
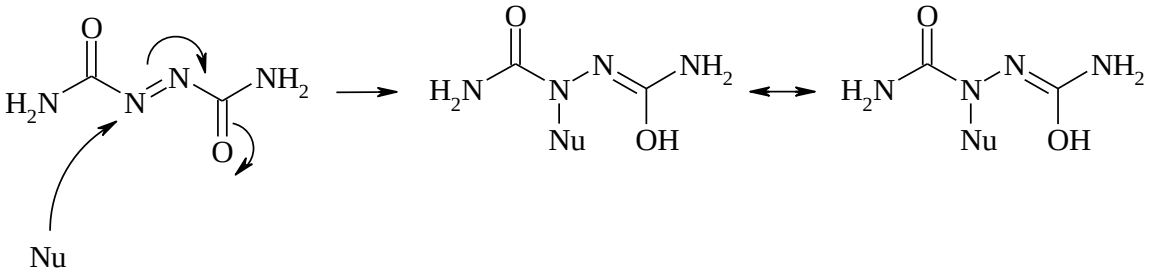
	R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

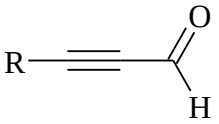
Individual profile/alert	
Name	Polarised alkene - pyrimidines
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding

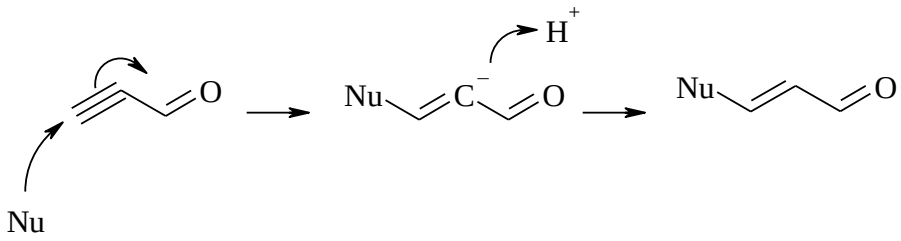
	rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

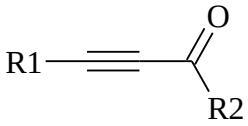
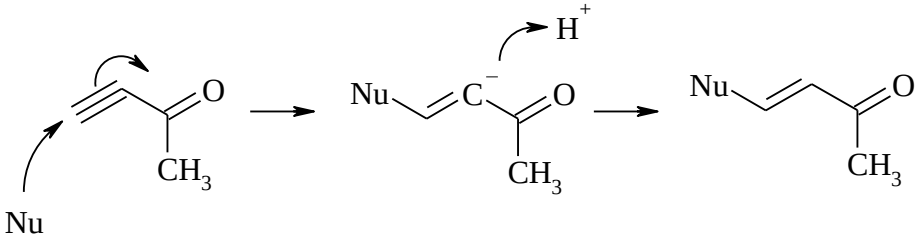
Individual profile/alert	
Name	Polarised alkene – triazines
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual

the profile (for each endpoint for the endpoint specific profilers)	toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

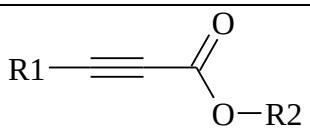
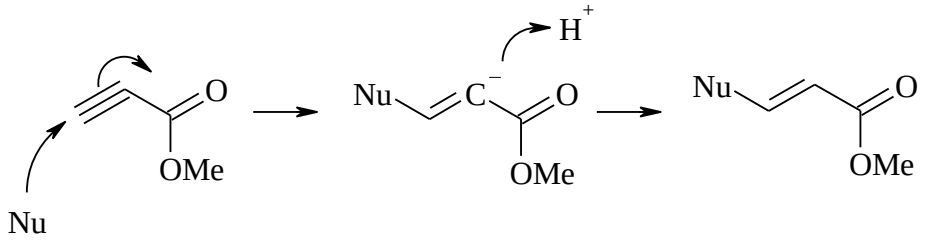
Individual profile/alert	
Name	Azocarbonamides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

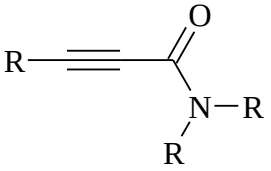
Individual profile/alert	
Name	Polarised alkyne - aldehydes
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible

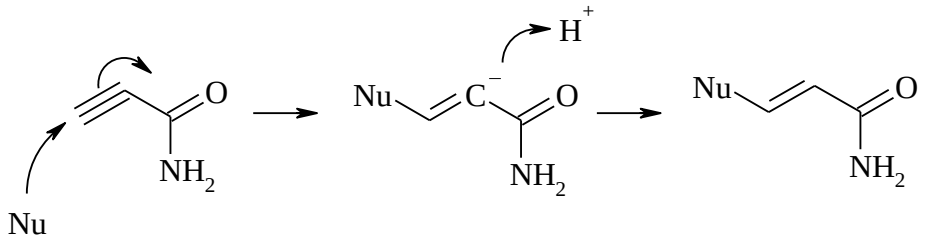
	for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

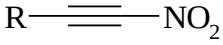
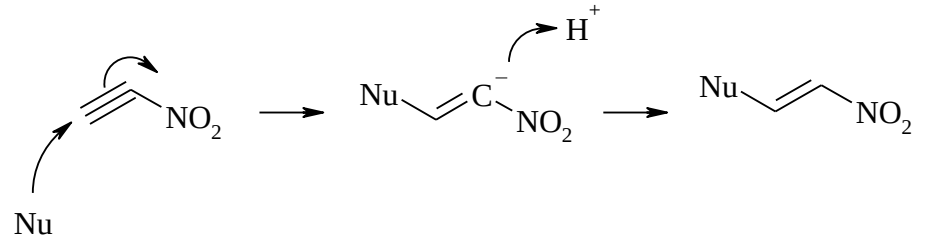
Individual profile/alert	
Name	Polarised alkyne - ketones
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.

Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

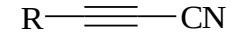
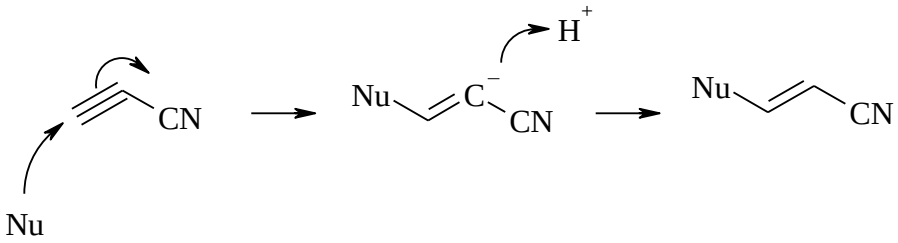
Individual profile/alert	
Name	Polarised alkyne - esters
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

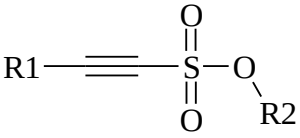
Individual profile/alert	
Name	Polarised alkyne - amides
Type of profile	Structural alert
Description/applicability domain	

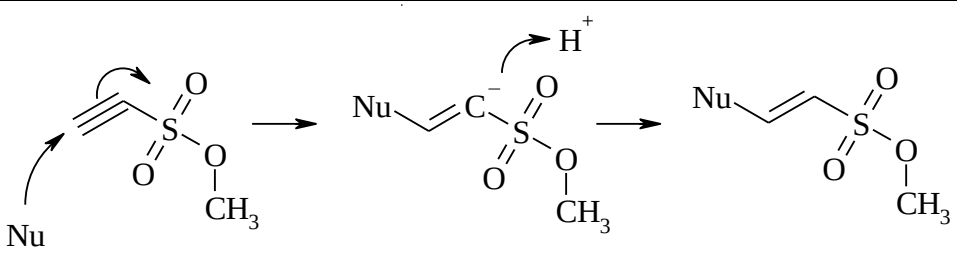
	R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkyne - nitros
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual

the profile (for each endpoint for the endpoint specific profilers)	toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

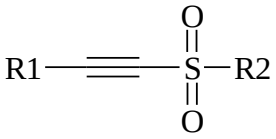
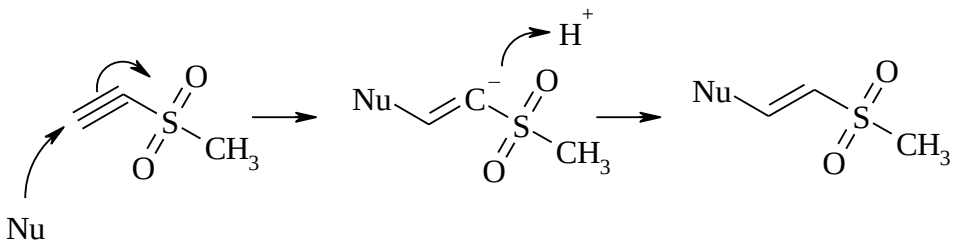
Individual profile/alert	
Name	Polarised alkyne - cyanos
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkyne - sulfonates
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

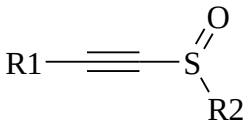
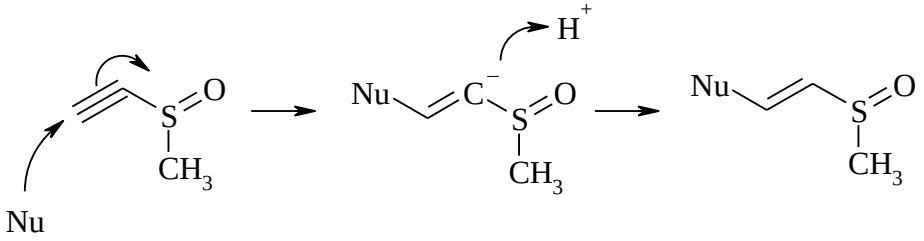


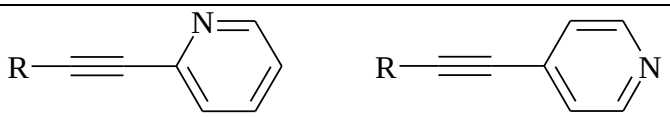
Nu = biological nucleophile

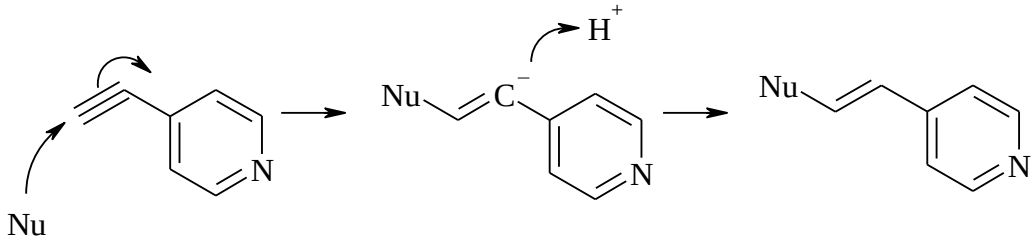
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

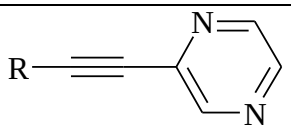
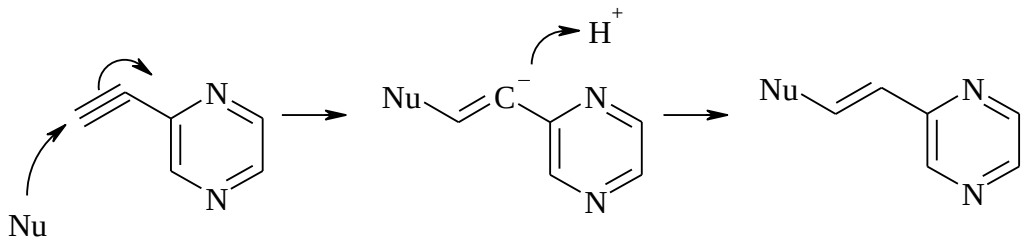
Individual profile/alert	
Name	Polarised alkyne - sulfones
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the	N/A – all alerts in this profiler were developed from a review of the

profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

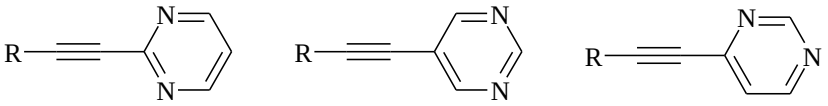
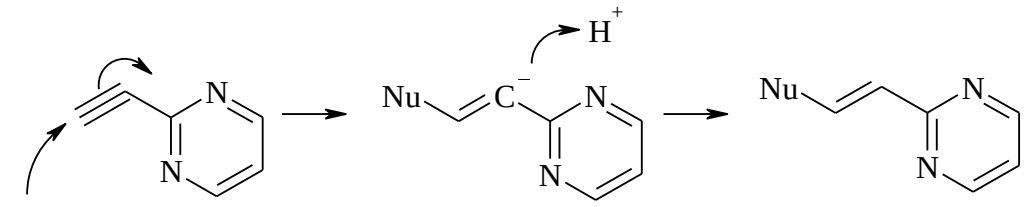
Individual profile/alert	
Name	Polarised alkyne - sulfinyls
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon or hydrogen R2 = any carbon
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkyne - pyridines
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

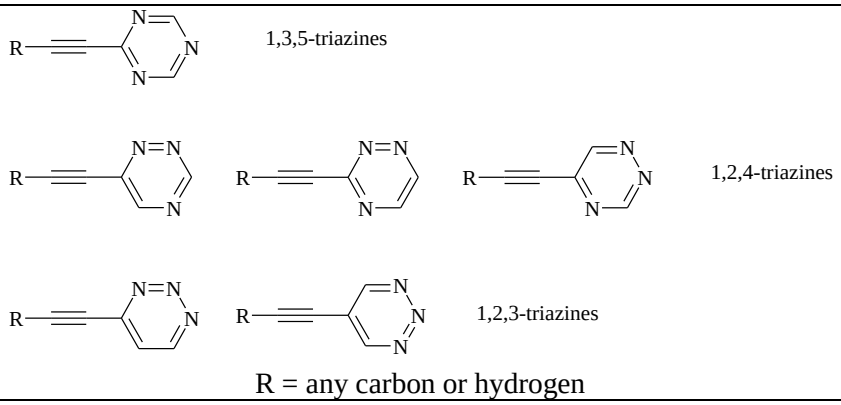
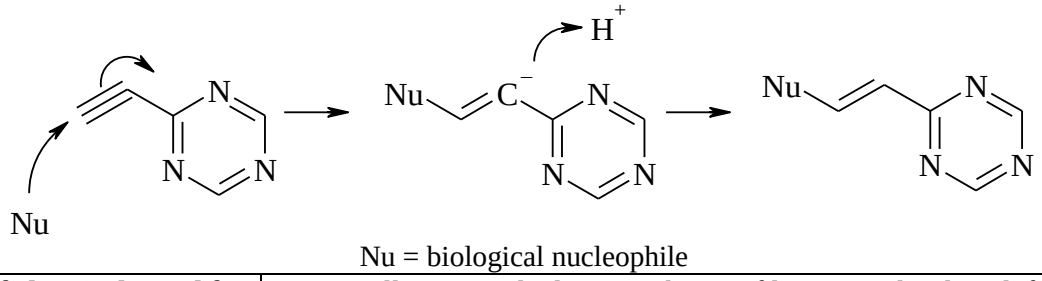
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

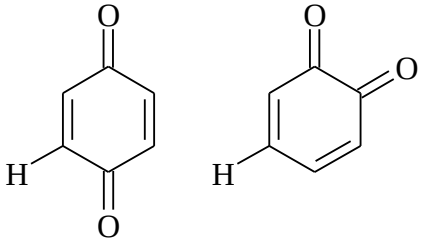
Individual profile/alert	
Name	Polarised alkyne - pyrazines
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual

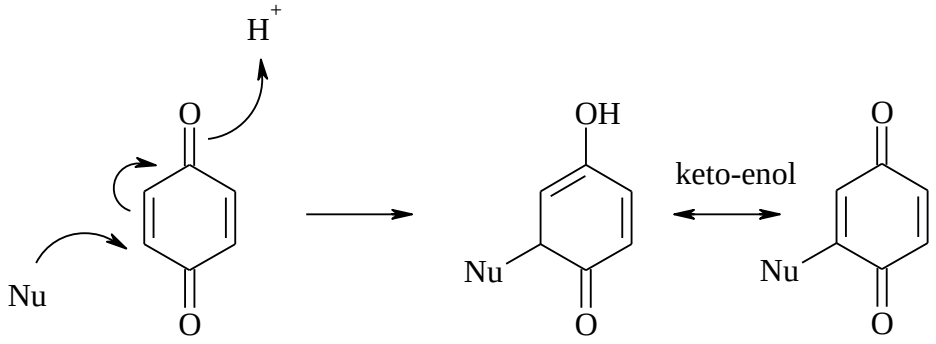
the profile (for each endpoint for the endpoint specific profilers)	toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkyne - pyrimidines
Type of profile	Structural alert
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkyne - triazines
Type of profile	Structural alert

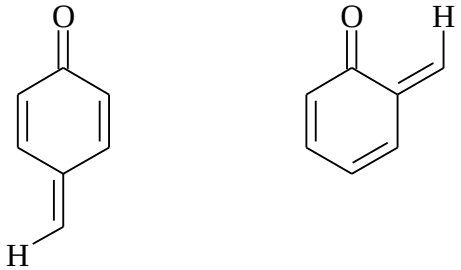
Description/applicability domain	
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

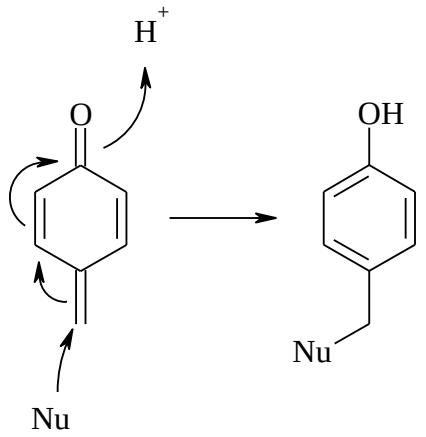
Individual profile/alert	
Name	Benzoquinones
Type of profile	Structural alert
Description/applicability domain	
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).



Nu = biological nucleophile

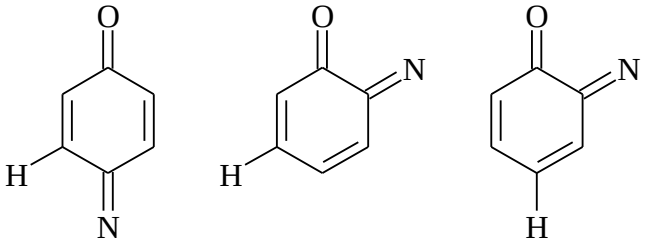
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

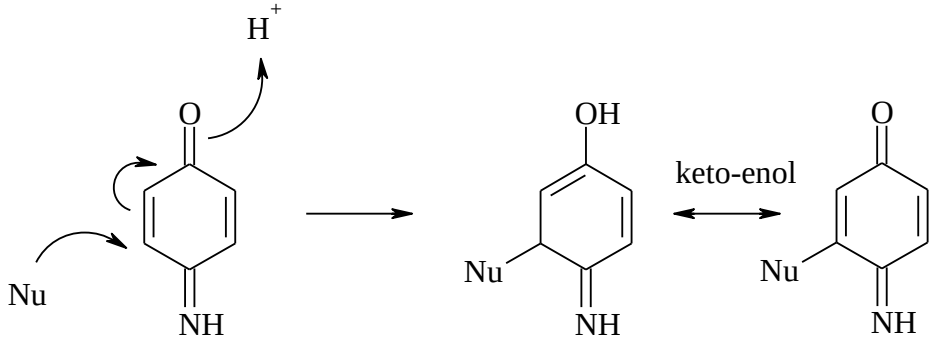
Individual profile/alert	
Name	Quinone-methides
Type of profile	Structural alert
Description/applicability domain	
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).



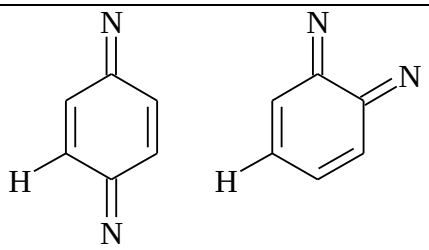
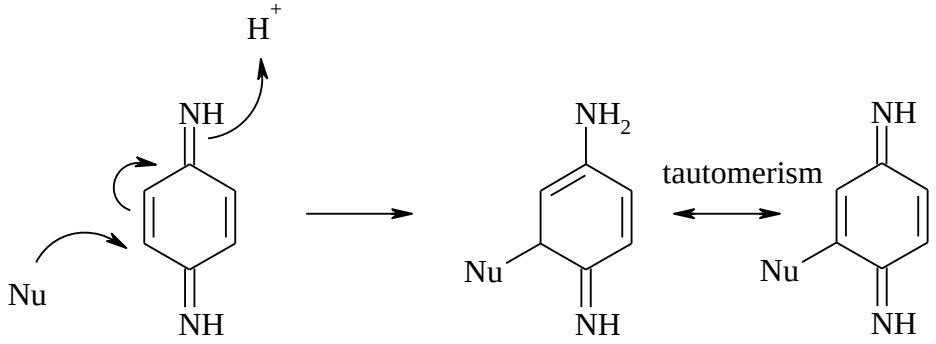
Nu = biological nucleophile

Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

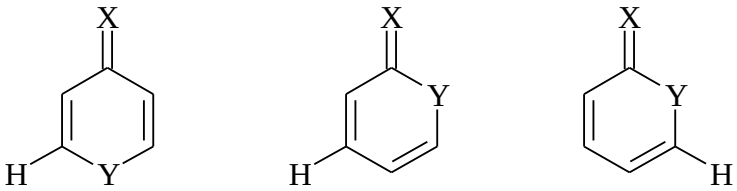
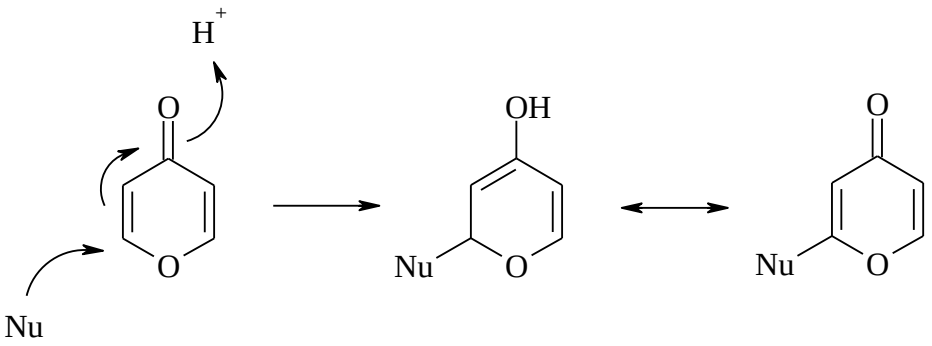
Individual profile/alert	
Name	Quinone-imines
Type of profile	Structural alert
Description/applicability domain	
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).



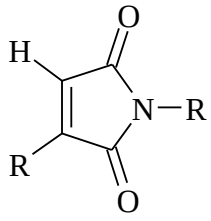
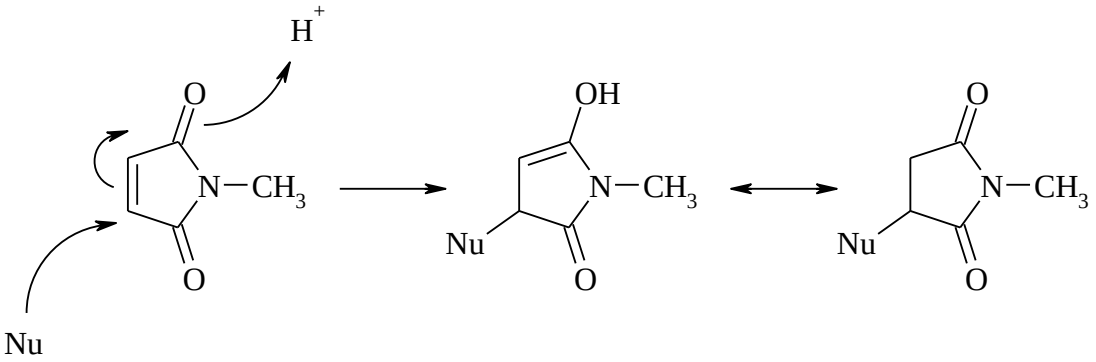
Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

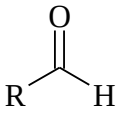
Individual profile/alert	
Name	Quinone-diimines
Type of profile	Structural alert
Description/applicability domain	
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.

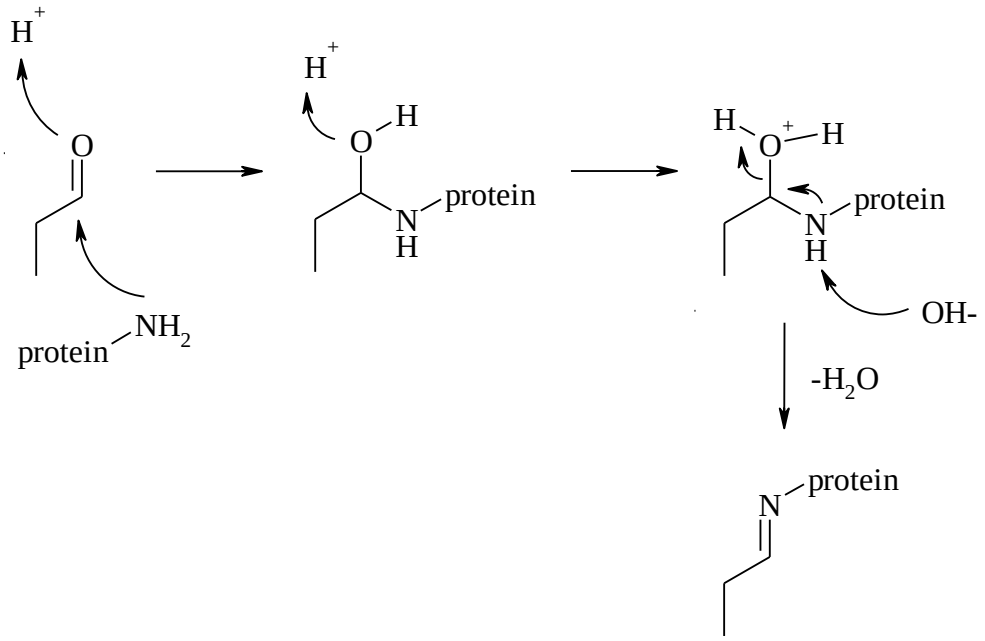
endpoint specific profilers)	
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Pyranones (and related nitrogen chemicals)
Type of profile	Structural alert
Description/applicability domain	 X = O, NH Y = O, N
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

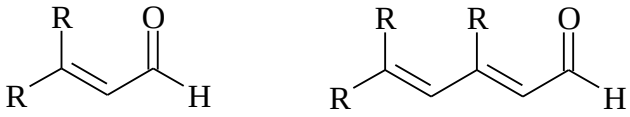
Individual profile/alert	
Name	Acid imides
Type of profile	Structural alert

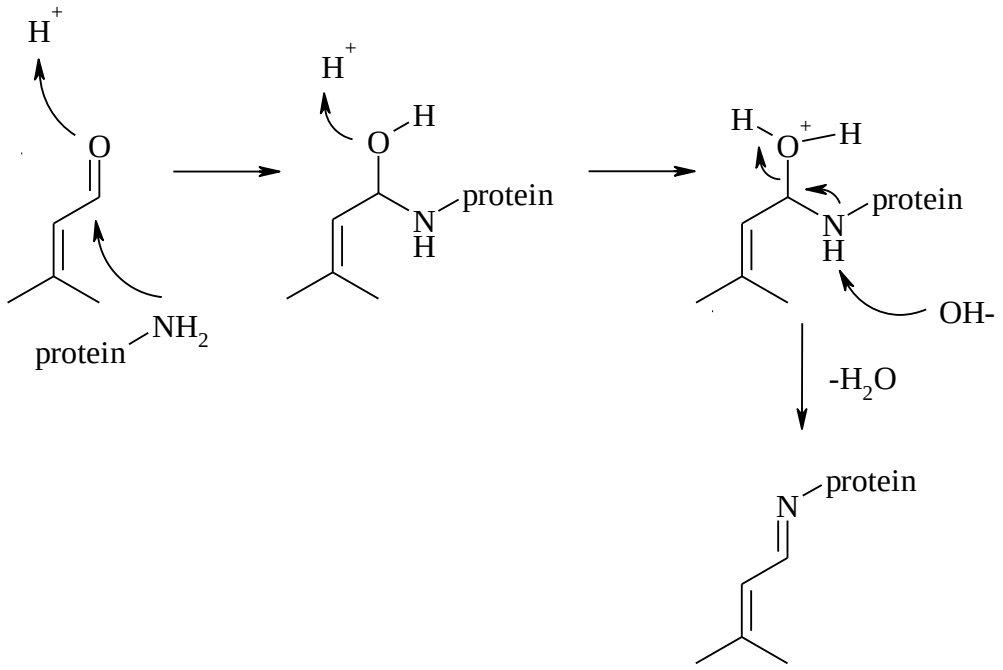
Description/applicability domain	 R = any carbon or hydrogen
Mechanism	A Michael addition mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Mono-carbonyls
Type of profile	Structural alert
Description/applicability domain	 R = hydrogen, any carbon (R groups cannot be aromatic, heteroaromatic or heterocyclic, unless they are either mono- or di-ortho-substituted, R cannot be carbonyl as these chemicals fall under a separate structural alert)
Mechanism	A Schiff base mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

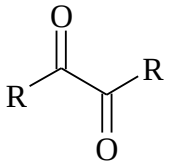


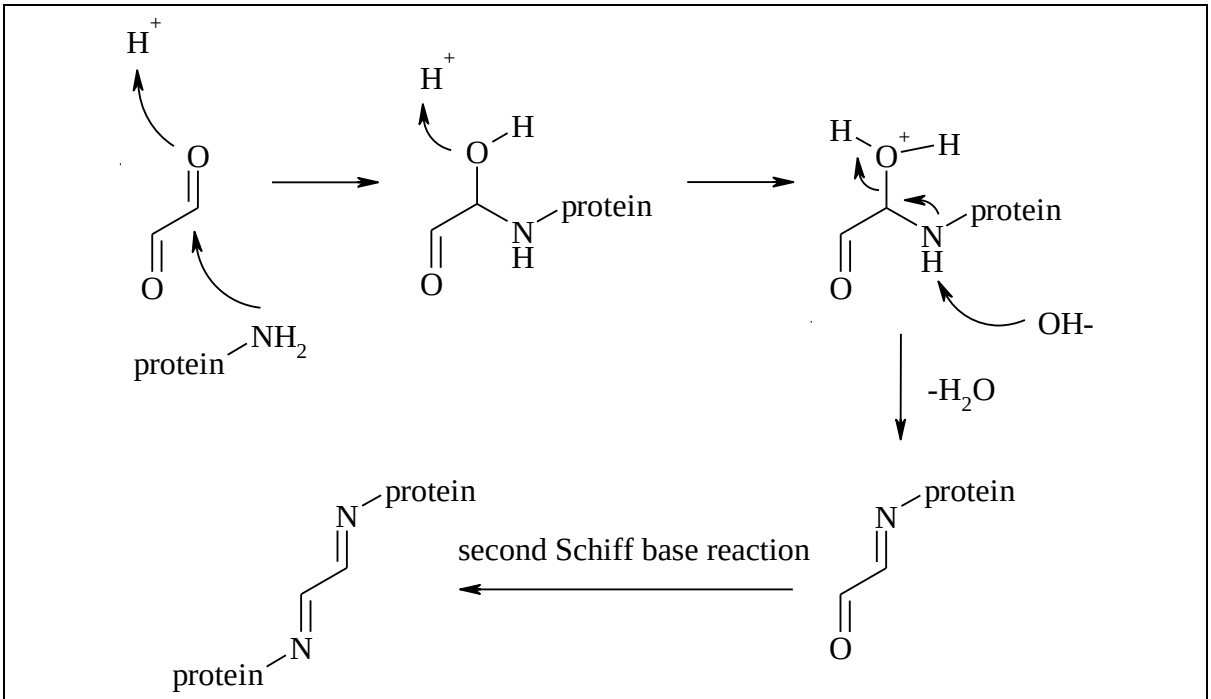
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Di-substituted α,β-unsaturated aldehydes
Type of profile	Structural alert
Description/applicability domain	 R = alkyl or aromatic carbon (including carbons in heterocyclic rings)
Mechanism	A Schiff base mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

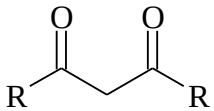


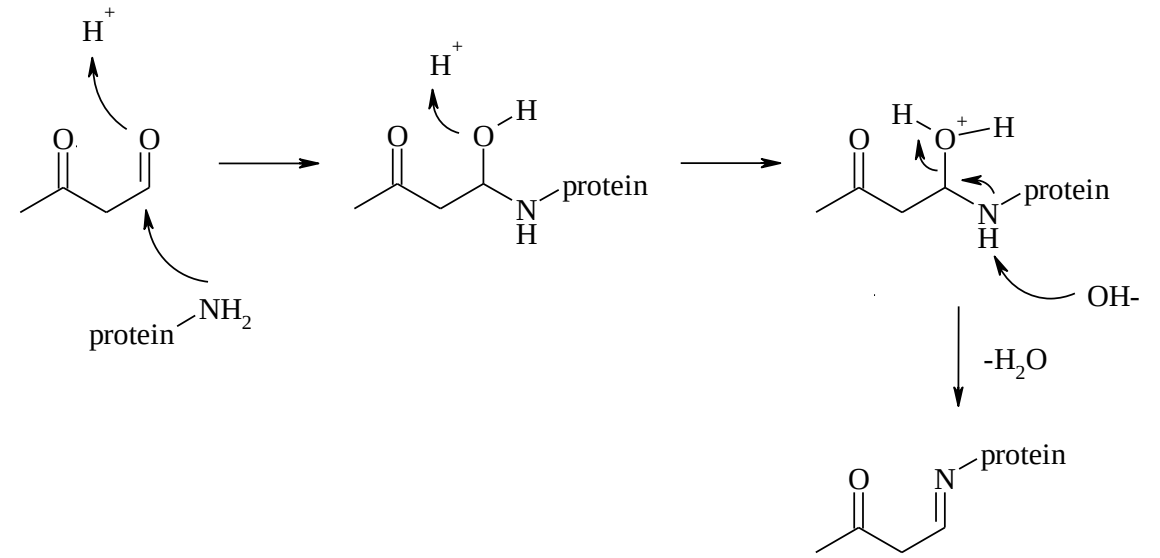
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	1,2-Dicarbonyls
Type of profile	Structural alert
Description/applicability domain	 R = hydrogen, any carbon (both R groups cannot be aromatic, heteroaromatic or heterocyclic, unless they are either mono- or di-ortho-substituted)
Mechanism	A Schiff base mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

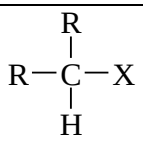
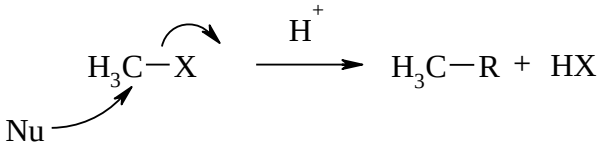


Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

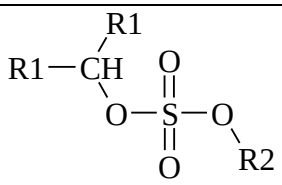
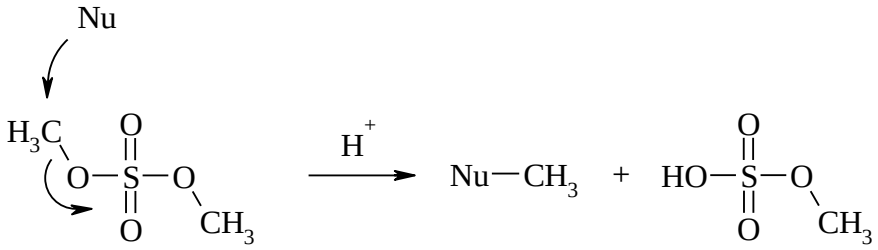
Individual profile/alert	
Name	1,3-Dicarbonyls
Type of profile	Structural alert
Description/applicability domain	 R = hydrogen, any carbon (both R groups cannot be aromatic, heteroaromatic or heterocyclic, unless they are either mono- or di-ortho-substituted)
Mechanism	A Schiff base mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

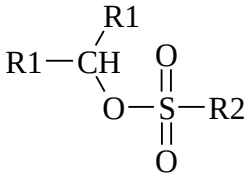
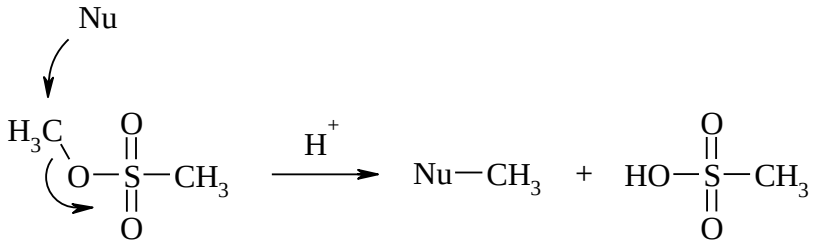


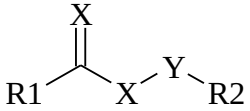
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

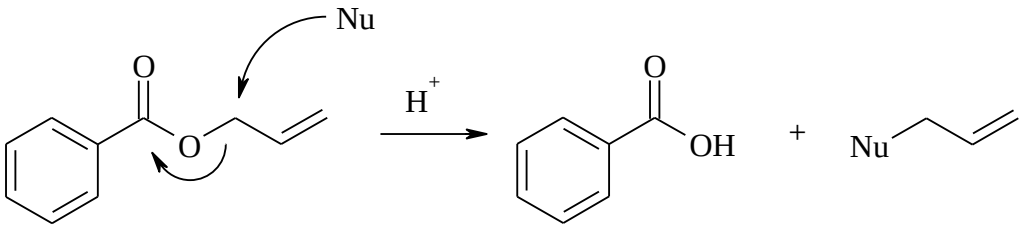
Individual profile/alert	
Name	Alkyl halides
Type of profile	Structural alert
Description/applicability domain	 R = hydrogen, any carbon except the following: R ≠ carbonyl (these chemicals fall under the α-halocarbonyl alert), -CS, -CN (these chemicals fall under the mustards alert) X = Cl, Br, I
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for	N/A – all structural alerts in this profiler were developed from a

profile development	review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Sulfates
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon, hydrogen R2 = any carbon Note: R1 and R2 can be part of an aliphatic ring system
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

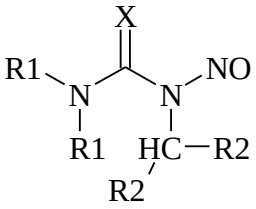
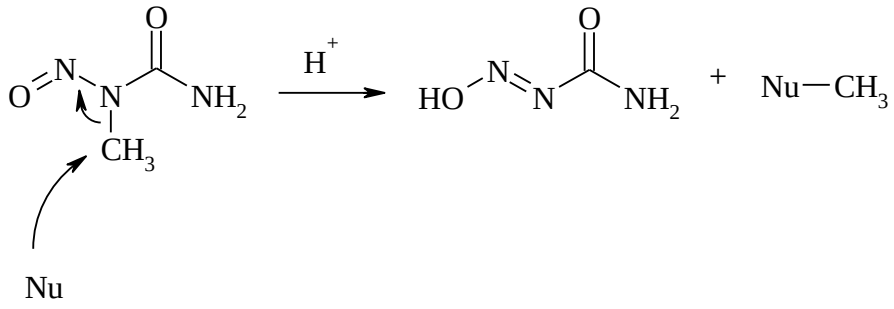
Individual profile/alert	
Name	Sulfonates
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon, hydrogen R2 = any carbon (R1 cannot be alkene or alkyne as these chemicals are Michael acceptors) Note: R1 and R2 can be part of an aliphatic ring system e.g. sultones
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Allyl acetates and related chemicals
Type of profile	Structural alert
Description/applicability domain	 X = oxygen, sulphur Y = CH_2, CH R1 = any carbon atom R2 = carbon atom part of an alkene, alkyne, aromatic ring, heteroaromatic ring or heterocyclic ring
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

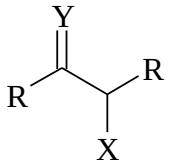
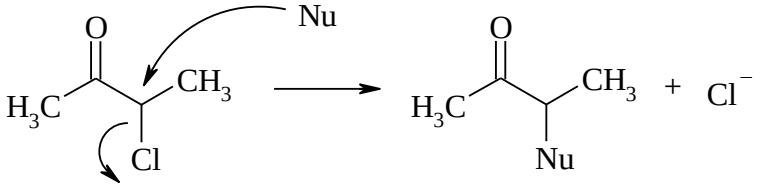


Nu = biological nucleophile

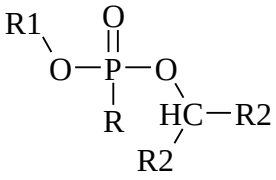
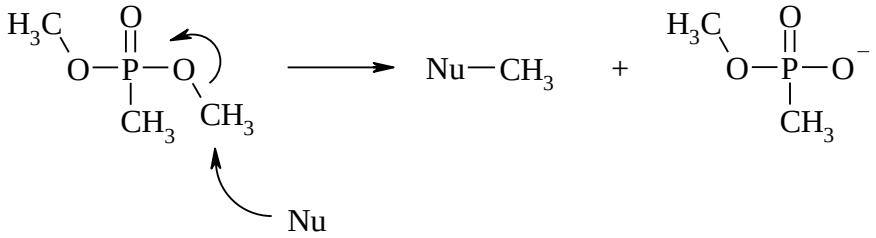
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

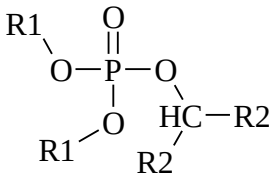
Individual profile/alert	
Name	Nitrosoureas (carbon)
Type of profile	Structural alert
Description/applicability domain	 X = oxygen (nitrosourea derivatives), nitrogen (nitrosoguanidine derivatives) R1 = any carbon, hydrogen R2 = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define

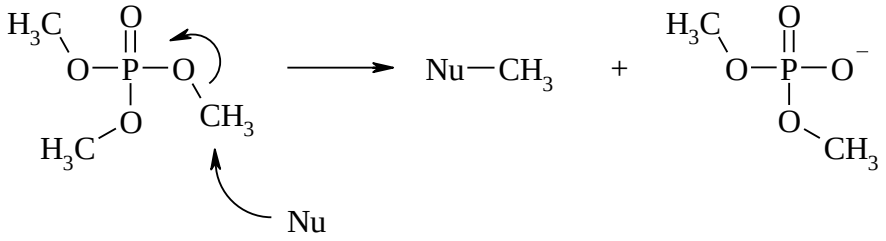
	the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	α-Halocarbonyls
Type of profile	Structural alert
Description/applicability domain	 Y = oxygen, sulphur X = halogen R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Phosphonates
Type of profile	Structural alert

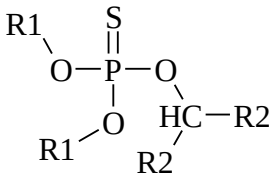
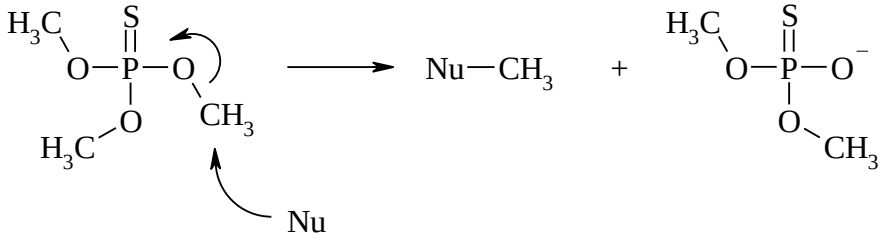
Description/applicability domain	 R1 = any carbon R2 = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Phosphates
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon, R2 = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

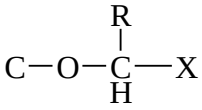
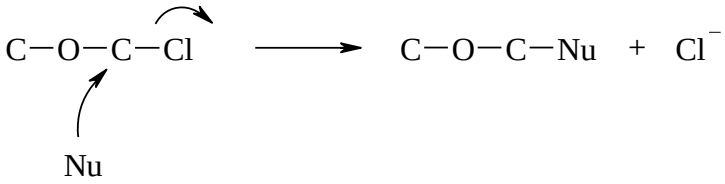


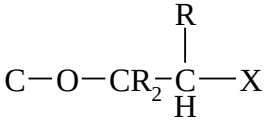
Nu = biological nucleophile

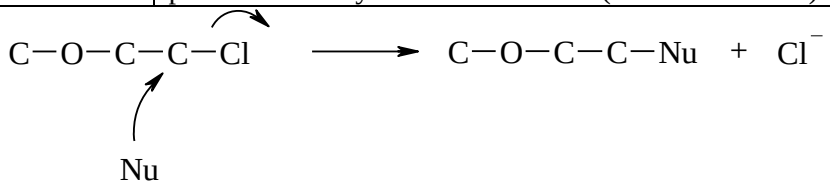
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

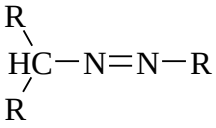
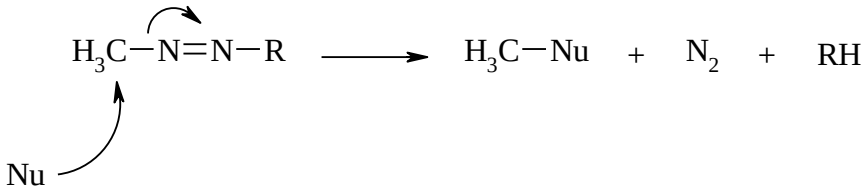
Individual profile/alert	
Name	Thiophosphates
Type of profile	Structural alert
Description/applicability domain	 R1 = any carbon R2 = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	 Nu = biological nucleophile
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.

Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

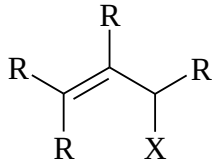
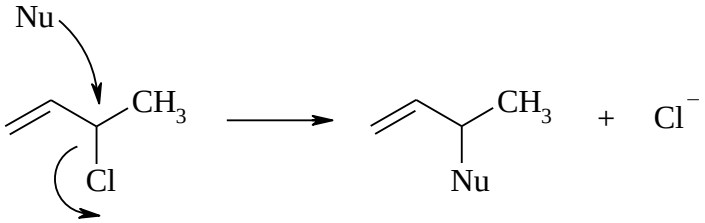
Individual profile/alert	
Name	α-Halo ethers
Type of profile	Structural alert
Description/applicability domain	 X = halogen R = any carbon atom, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

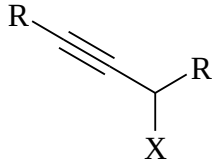
Individual profile/alert	
Name	β-Halo ethers
Type of profile	Structural alert
Description/applicability domain	 X = halogen R = any carbon atom, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the

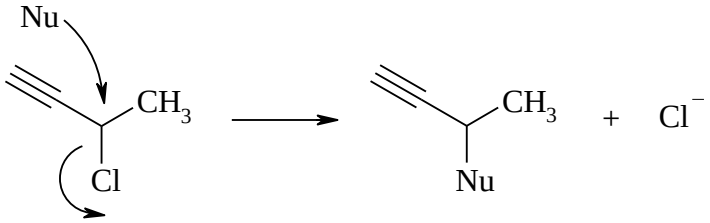
	protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

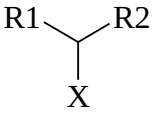
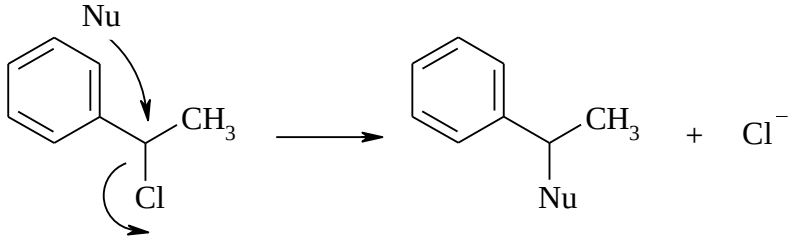
Individual profile/alert	
Name	Alkyl diazos
Type of profile	Structural alert
Description/applicability domain	 X = halogen R = any carbon atom, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the

endpoint for the endpoint specific profilers)	alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

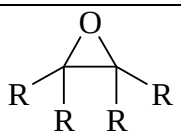
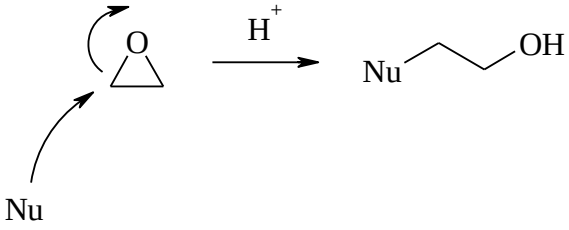
Individual profile/alert	
Name	α-Haloalkenes (and related cyano, sulfate and sulphonate substituted chemicals)
Type of profile	Structural alert
Description/applicability domain	 X = halogen, cyano, sulfate, sulphonate R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	α-Haloalkynes (and related cyano, sulfate and sulphonate substituted chemicals)
Type of profile	Structural alert
Description/applicability domain	

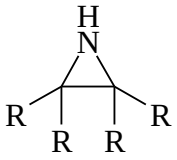
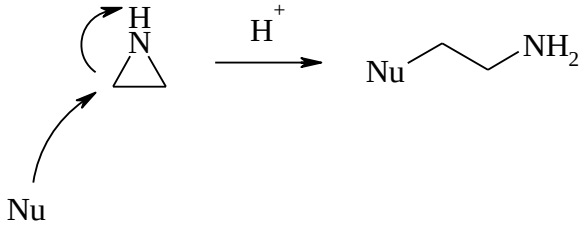
	X = halogen, cyano, sulfate, sulphonate R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

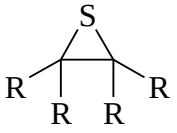
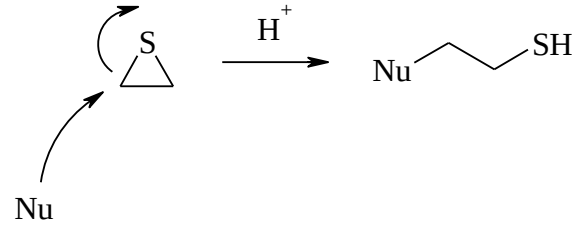
Individual profile/alert	
Name	α-Halobenzyls (and related cyano, sulfate and sulphonate substituted chemicals)
Type of profile	Structural alert
Description/applicability domain	 X = halogen, cyano, sulfate, sulphonate R1 = aromatic carbon R2 = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the

	molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

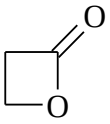
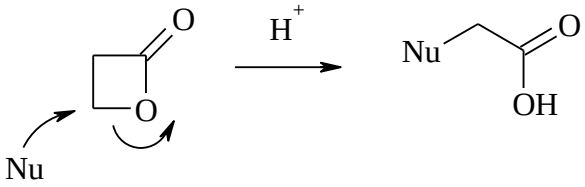
Individual profile/alert	
Name	Epoxides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Aziridines
Type of profile	Structural alert

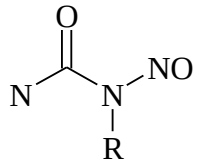
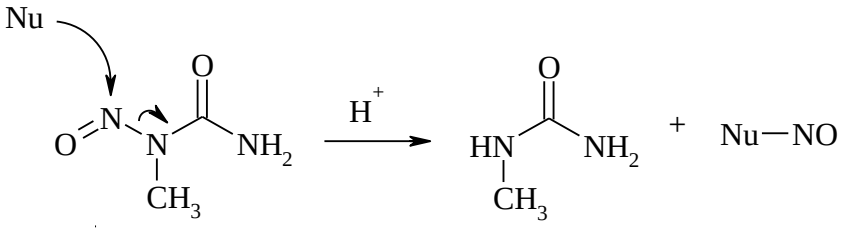
Description/applicability domain	 R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

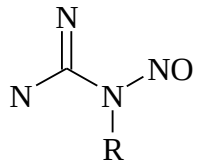
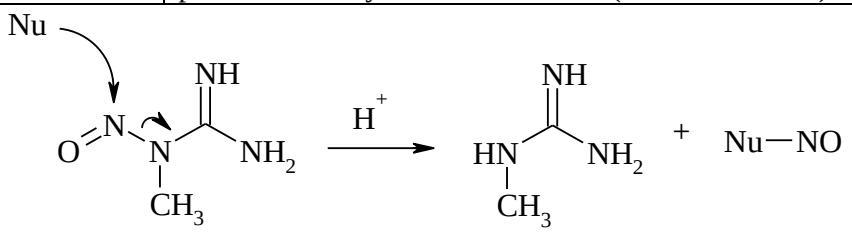
Individual profile/alert	
Name	Sulfuranes
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define

	the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

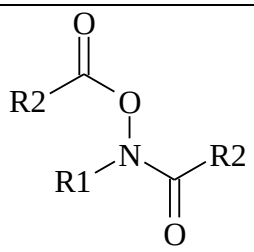
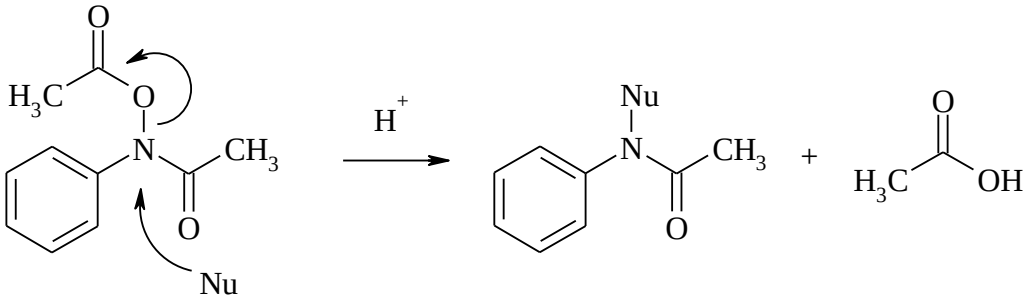
Individual profile/alert	
Name	β-Lactones
Type of profile	Structural alert
Description/applicability domain	
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Nitrosoureas (nitrogen)
Type of profile	Structural alert

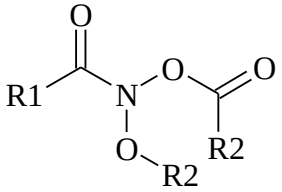
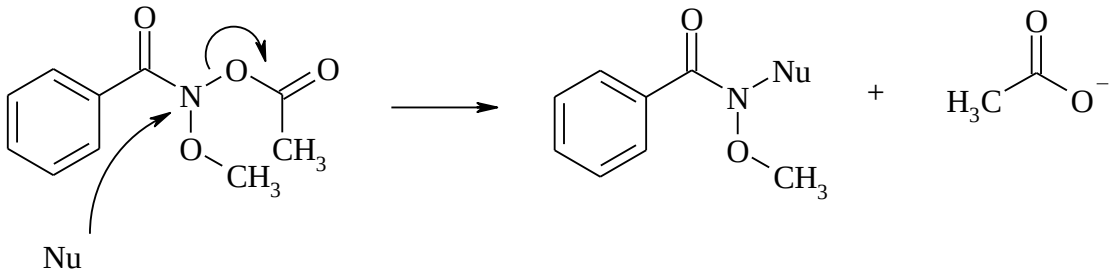
Description/applicability domain	 R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

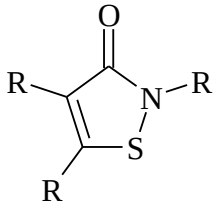
Individual profile/alert	
Name	Nitrosoguanidines (nitrogen)
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for	N/A – all structural alerts in this profiler were developed from a

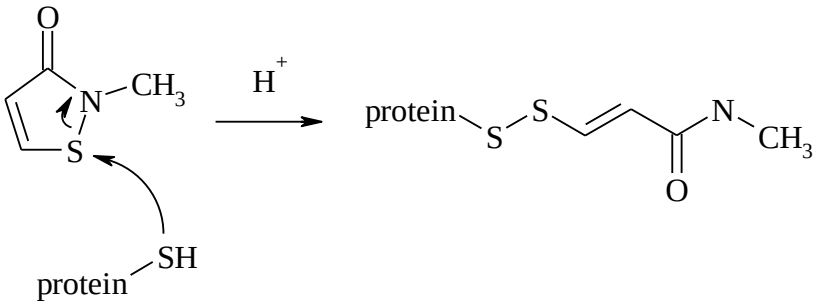
profile development	review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

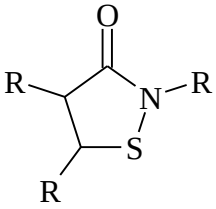
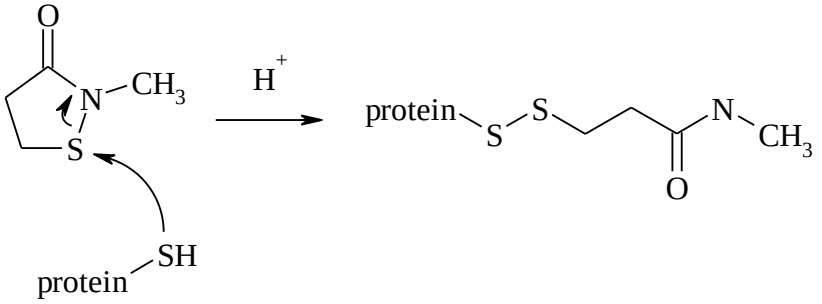
Individual profile/alert	
Name	*N*-Acetoxy-*N*-acetyl-phenyl
Type of profile	Structural alert
Description/applicability domain	 R1 = aromatic, heteroaromatic, heterocyclic ring system R2 = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.

profilers)	
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

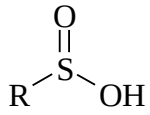
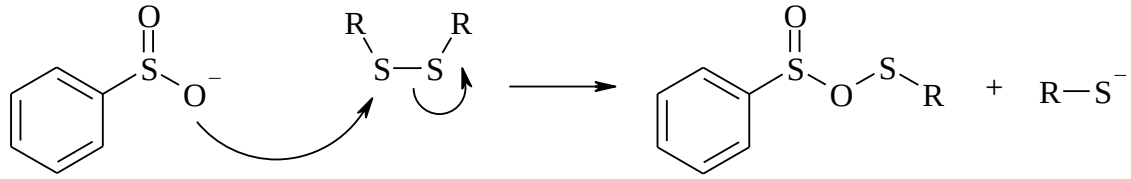
Individual profile/alert	
Name	*N*-Acyloxy-*N*-alkoxyamides
Type of profile	Structural alert
Description/applicability domain	 R1 = aromatic, heteroaromatic, heterocyclic ring system R2 = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

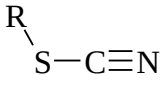
Individual profile/alert	
Name	Isothiazol-3-ones (sulphur)
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, hydrogen, halogen

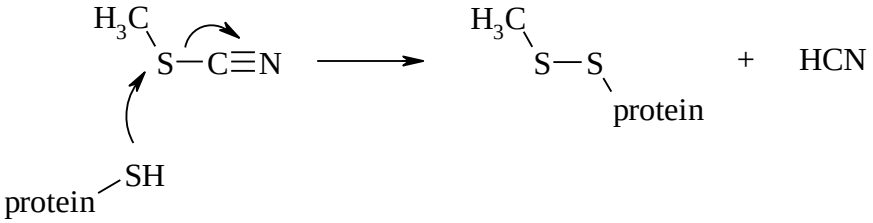
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

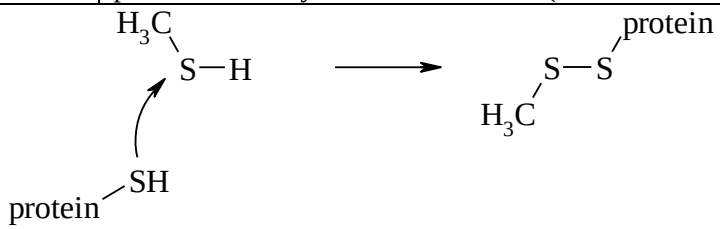
Individual profile/alert	
Name	Isothiazolin-3-ones (sulphur)
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, hydrogen, halogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the

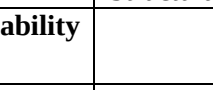
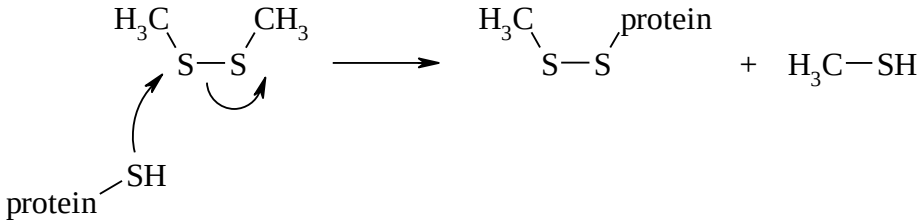
	molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

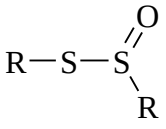
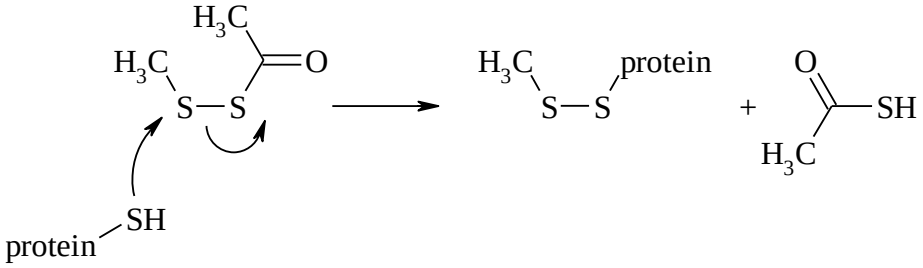
Individual profile/alert	
Name	Aromatic sulphonic acids
Type of profile	Structural alert
Description/applicability domain	 R = aromatic, heteroaromatic, heterocyclic ring system
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Thiocyanates
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the

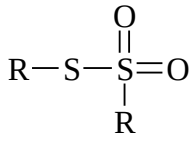
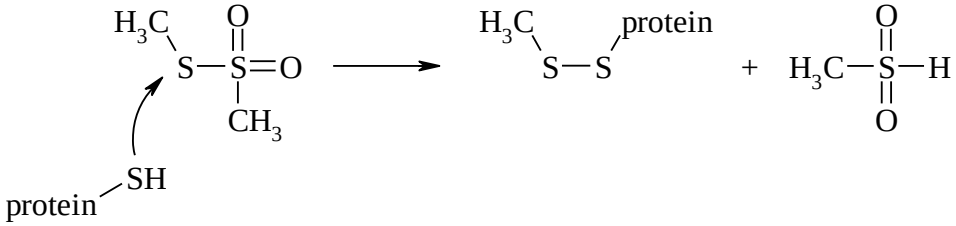
	protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

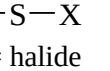
Individual profile/alert	
Name	Thiols
Type of profile	Structural alert
Description/applicability domain	R—SH R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

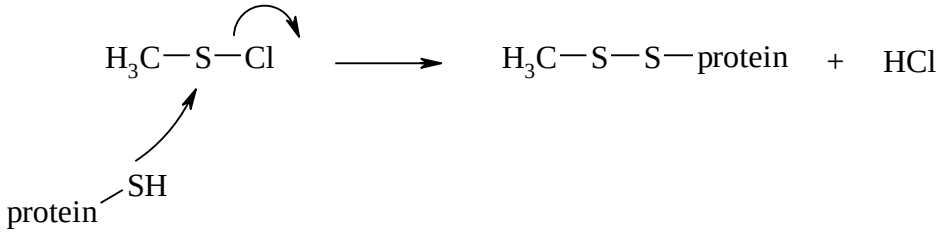
Individual profile/alert	
Name	Disulfides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

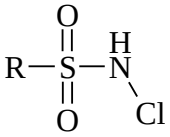
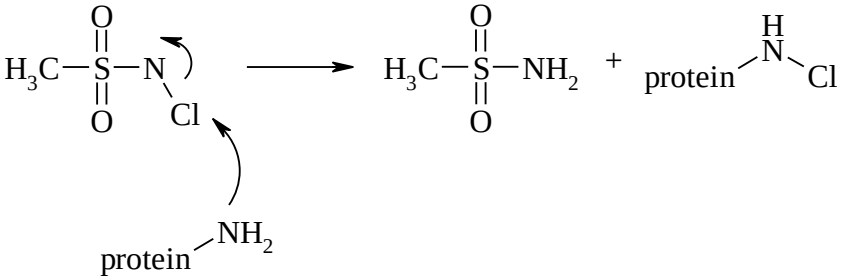
Individual profile/alert	
Name	Thiosulfonates
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define

	the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

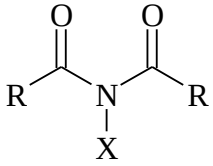
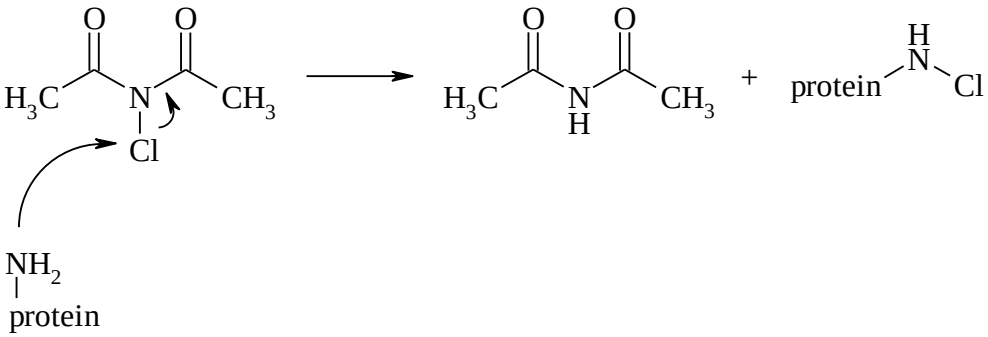
Individual profile/alert	
Name	Sulfoxides of disulfides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Sulfenyl halides
Type of profile	Structural alert
Description/applicability domain	 X = halide

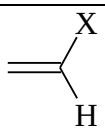
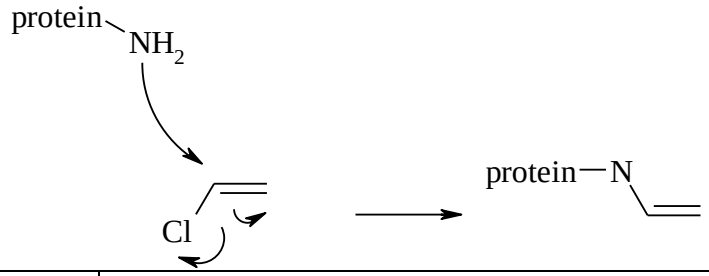
	R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

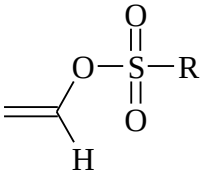
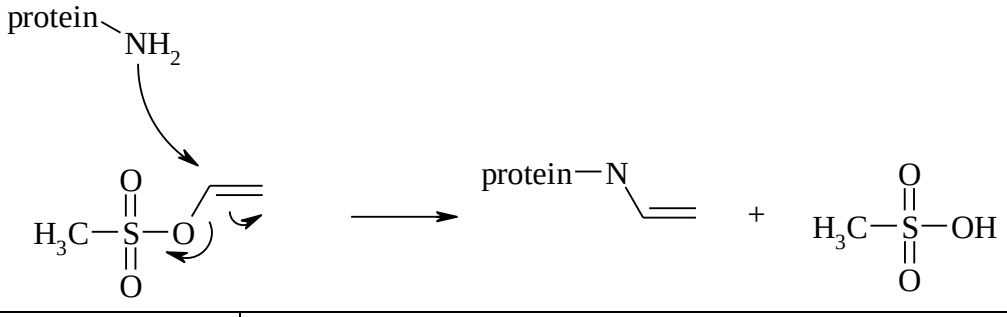
Individual profile/alert	
Name	*N*-Chloro-sulphonamides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.

Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

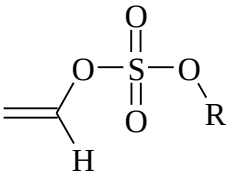
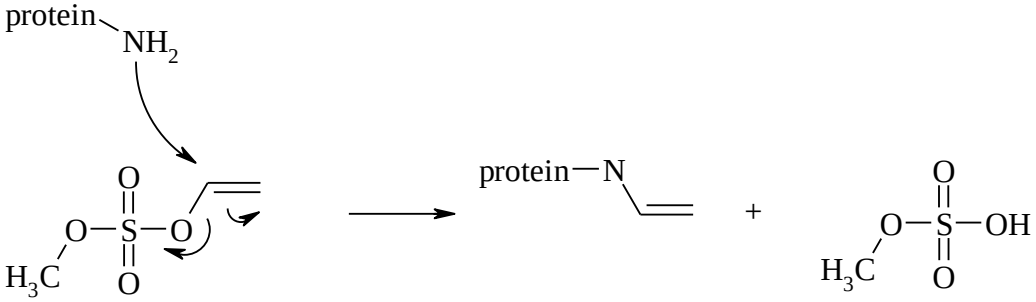
Individual profile/alert	
Name	*N*-Haloimides
Type of profile	Structural alert
Description/applicability domain	 R = any carbon, hydrogen X = F, Cl, Br, I
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

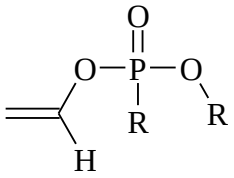
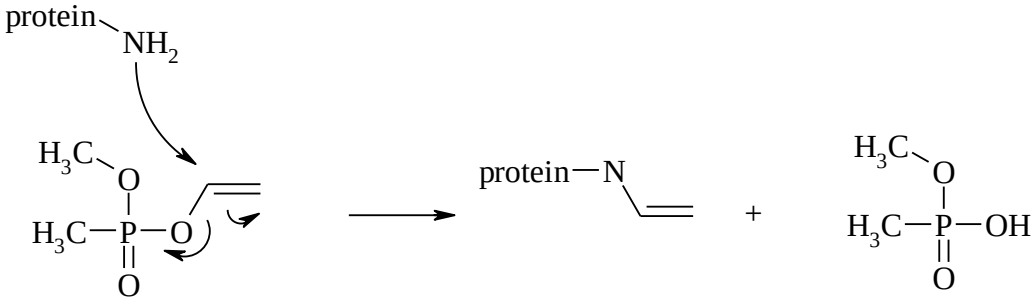
Individual profile/alert	
Name	Polarised alkenes with a halogen leaving group
Type of profile	Structural alert

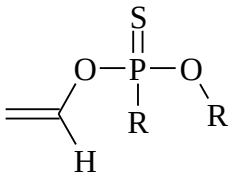
Description/applicability domain	 X = F, Cl, Br, I
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

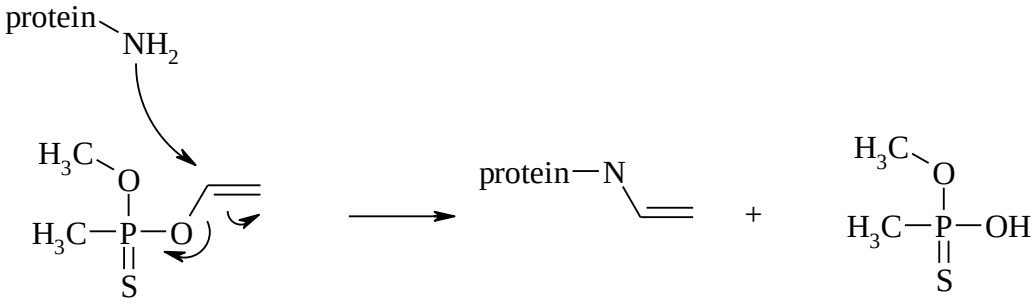
Individual profile/alert	
Name	Polarised alkenes with a sulfonate leaving group
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for	N/A – all structural alerts in this profiler were developed from a

profile development	review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

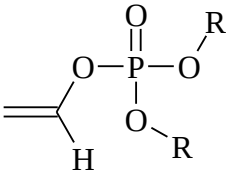
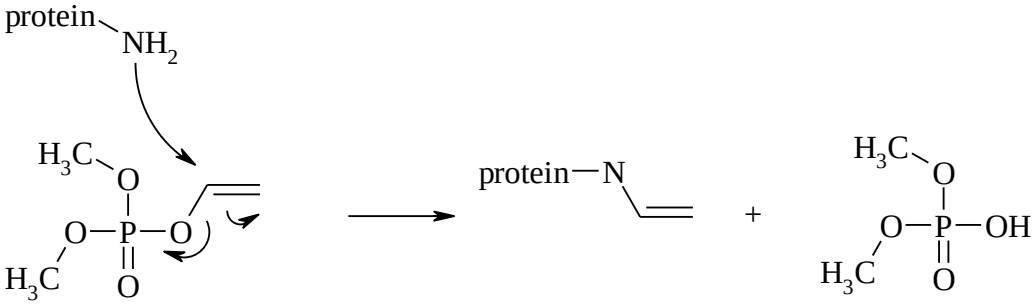
Individual profile/alert	
Name	Polarised alkenes with a sulfate leaving group
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkenes with a phosphonate leaving group
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

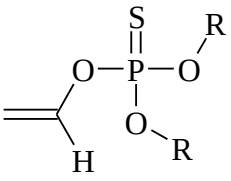
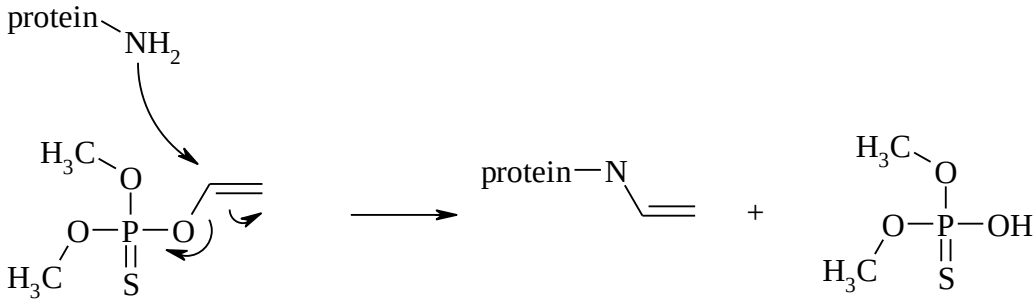
Individual profile/alert	
Name	Polarised alkenes with a thiophosphonate leaving group
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).



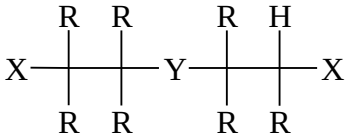
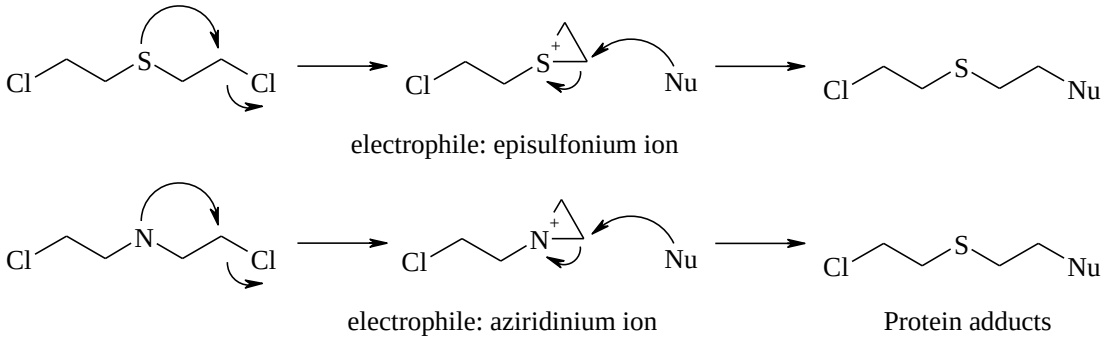
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

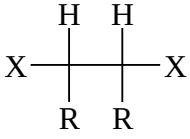
Individual profile/alert	
Name	Polarised alkenes with a phosphate leaving group
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined

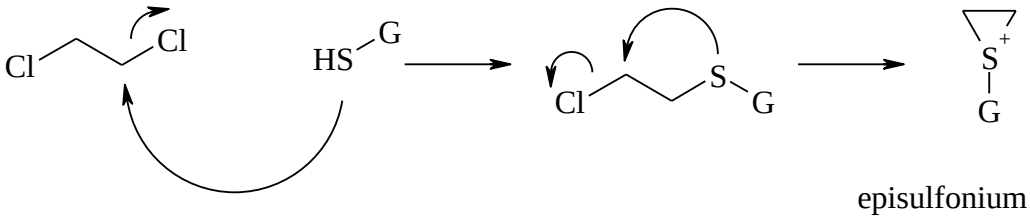
	and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Polarised alkenes with a thiophosphate leaving group
Type of profile	Structural alert
Description/applicability domain	 R = any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Mustards
Type of profile	Structural alert

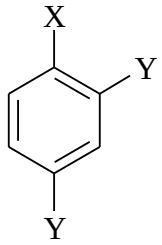
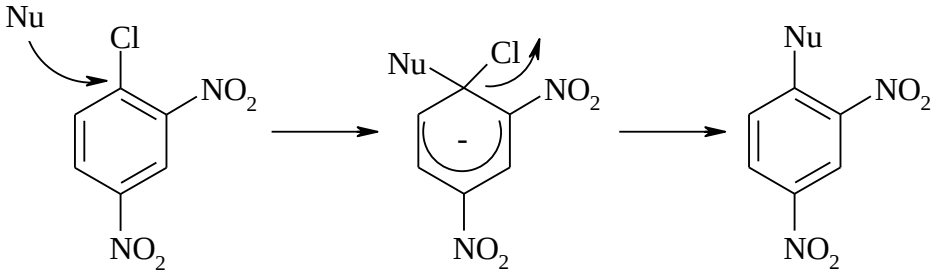
Description/applicability domain	 Y = nitrogen, sulphur (any oxidation state of sulphur is allowed as long as a lone pair remains free for the cyclisation reaction) X = Cl, Br, I R = any carbon, hydrogen
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 electrophile: episulfonium ion electrophile: aziridinium ion Protein adducts	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	1,2-Dihaloalkanes
Type of profile	Structural alert
Description/applicability domain	 X = Cl, Br, I R = hydrogen, any carbon
Mechanism	An S_N2 mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).

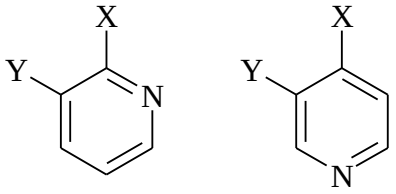
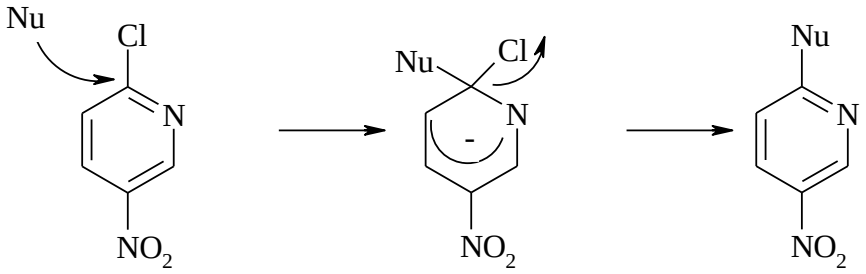


episulfonium ion

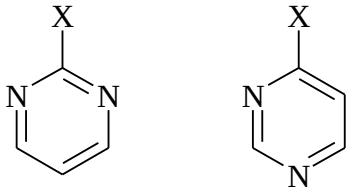
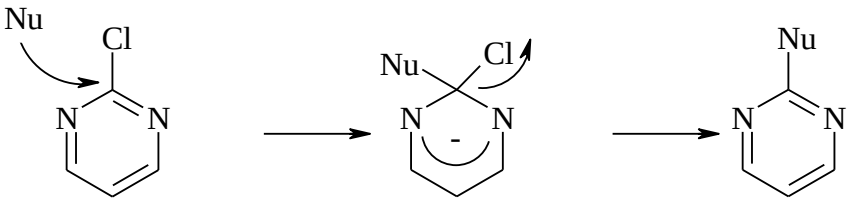
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

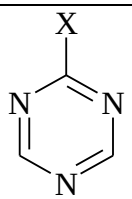
Individual profile/alert	
Name	Activated halo-benzenes
Type of profile	Structural alert
Description/applicability domain	 X (leaving group) = F, Cl, Br, I, CN Y (activating group) = aldehyde, nitro, cyano, halogen, sulfinyl, sulfone, sulfonate, trifluoromethyl
Mechanism	A S_NAr mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define

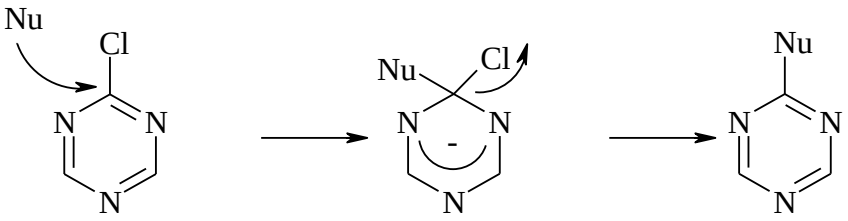
	the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Activated halo-pyridines
Type of profile	Structural alert
Description/applicability domain	 X (leaving group) = F, Cl, Br, I, CN Y (activating group) = aldehyde, nitro, cyano, halogen, sulfinyl, sulfone, sulfonate, trifluoromethyl
Mechanism	An S_NAr mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.

References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Halo-pyrimidines
Type of profile	Structural alert
Description/applicability domain	 X (leaving group) = F, Cl, Br, I, CN
Mechanism	An S_NAr mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).
 Nu = biological nucleophile	
Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802

Individual profile/alert	
Name	Halo-triazines
Type of profile	Structural alert
Description/applicability domain	 X (leaving group) = F, Cl, Br, I, CN
Mechanism	An S_NAr mechanism has been suggested to be responsible for the protein reactivity of these chemicals (Enoch et al 2010).



Nu = biological nucleophile

Set of chemicals used for profile development	N/A – all structural alerts in this profiler were developed from a review of the electrophilic chemistry associated with covalent protein binding rather than an analysis of toxicological data. The alerts define the chemistry for endpoints where covalent binding to a protein is the molecular initiating event.
Data/Knowledge used for profile development	An extensive review of the literature was performed enabling the chemistry associated with covalent binding to a protein to be defined and encoded in this profiler.
Performance of the profile / or Analysis of the profile (for each endpoint for the endpoint specific profilers)	N/A – all alerts in this profiler were developed from a review of the chemistry associated with covalent a protein binding. Individual toxicological datasets were not analysed during the development of the alerts within this profiler.
References	Enoch et al (2010) Critical Reviews in Toxicology, 41, p783-802