The second filter (**MCF-2**), based on 30 groups, flags chemotypes proven to impart acute or chronic toxicity. The applicability of this filter is conditional on the purpose of libraries design. For instance, a library targeted against metal-containing enzymes (MMP, PDF, HAD, etc) should include compounds with all types of chelating groups (hydroxamic acids, thiols, oximes, etc.).

Chemotype	Potential Liabilities	Chemotype	Potential Liabilities
α- and β-Napthylamines	Carcinogenic	Aminals, acetals, thioacetal, mix	PK unstable
Cyclic and linear thioureas	ADME problems Nonspecific protein binding	Polyaromatics (anthracenes, phenanthrenes, etc.)	Intercalators
Crown ethers	Non-targeted	Oxime and oxime ethers	PK unstable
Hydrazones	Aggregation phenomena PK unstable	Barbiturates	Nonspecific
Steroid like	Nonspecific	Diastereomeric mixtures	Nonselective
Michael acceptors	Aggregation phenomena PK unstable Nonspecific protein binding	Positively charged *N*-heterocycles	ADME problems
Thiols	PK unstable Nonspecific protein binding	Nitrobenzenes	ADME problems, toxicity
Polypeptides	ADME problems	Phenylenediamines	Carcinogenic, toxicity
Heterocyclic *N*-oxides	ADME problems	Amidine or guanidine	PK unstable
Mannich products	PK unstable	Hydroxamic acids and derivatives	PK unstable
Dioxines, dibenzofuranes	Carcinogenic	Long aliphatic chain (> 8 CH_2)	ADME problems
Nonsubstituted adamantane fragment	ADME problems	Polyfluorinated chains (“Teflon”compounds)	ADME problems
Polyhaloaromatics	ADME problems, toxicity	Cyclic alkylating agents	Carcinogenic, toxicity
Nitroheterocycles (nitrofuranes)	Non-targeted toxicity	Ferrocenes and similar	ADME problems
Disulfides	PK unstable Nonspecific protein binding	Nucleotide-like	ADME problems