

## Supplementary Information

**Table S1.** Comparison of prediction outcomes of QSAR and multiple alerts generated by the OECD QSAR Toolbox for marketed and withdrawn drugs.

Drug Name	State	QSAR predictions <sup>1</sup>	Toxic hazard classification by Cramer (extension) <sup>2</sup>	Toxic hazard classification by Cramer (original) <sup>2</sup>	Carcinogenicity (genotox and nongenotox) alerts by ISS <sup>2</sup>	DNA alerts for AMES, MN and CA by OASIS v.1.3 <sup>2</sup>	<i>In vitro</i> mutagenicity (Ames test) alerts by ISS <sup>2</sup>	<i>In vivo</i> mutagenicity (micronucleus) alerts by ISS <sup>2</sup>	Protein binding alerts for chromosomal aberration by OASIS v1.1 <sup>2</sup>	Protein binding alerts for skin sensitization by OASIS v1.3 <sup>2</sup>
Amineptine	withdrawn	unsafe	High (Class III)	High (Class III)	No alert found	No alert found	No alert found	Alerts	No alert found	No alert found
Duract	withdrawn	unsafe	High (Class III)	High (Class III)	No alert found	No alert found	No alert found	Alerts	No alert found	No alert found
Vioxx	withdrawn	unsafe	High (Class III)	High (Class III)	No alert found	No alert found	No alert found	Alerts	No alert found	Alerts
Astemizole	withdrawn	unsafe	High (Class III)	High (Class III)	Alerts	No alert found	No alert found	Alerts	No alert found	No alert found
Cerivastatin	withdrawn	unsafe	High (Class III)	High (Class III)	No alert found	No alert found	No alert found	Alerts	No alert found	No alert found
Chlormezanone	withdrawn	unsafe	High (Class III)	High (Class III)	Alerts	No alert found	No alert found	Alerts	No alert found	No alert found
Fenfluramine	withdrawn	unsafe	High (Class III)	High (Class III)	No alert found	No alert found	No alert found	No alert found	No alert found	No alert found
Flosequinan	withdrawn	unsafe	High (Class III)	High (Class III)	Alerts	No alert found	Alerts	Alerts	Alerts	Alerts
Glafenine	withdrawn	unsafe	High (Class III)	High (Class III)	Alerts	No alert found	No alert found	Alerts	No alert found	No alert found
Grepafloxacin	withdrawn	unsafe	High (Class III)	High (Class III)	Alerts	No alert found	No alert found	Alerts	Alerts	No alert found
Mibefradil	withdrawn	unsafe	High (Class III)	High (Class III)	Alerts	No alert found	No alert found	Alerts	No alert found	No alert found

Troglitazone	withdrawn	unsafe	<b>High (Class III)</b>	<b>High (Class III)</b>	No alert found	No alert found	No alert found	<b>Alerts</b>	No alert found	No alert found
Ximelagatran	withdrawn	unsafe	<b>High (Class III)</b>	<b>High (Class III)</b>	No alert found	<b>Alerts</b>	No alert found	<b>Alerts</b>	No alert found	No alert found
Aspirin	marketed	safe	Low (Class I)	Low (Class I)	No alert found	No alert found	No alert found	<b>Alerts</b>	No alert found	<b>Alerts</b>
Ibuprofen	marketed	safe	Low (Class I)	Low (Class I)	No alert found	No alert found	No alert found	<b>Alerts</b>	No alert found	No alert found
Valtrex	marketed	safe	<b>High (Class III)</b>	<b>High (Class III)</b>	No alert found	No alert found	No alert found	<b>Alerts</b>	No alert found	<b>Alerts</b>
Microzide	marketed	safe	<b>High (Class III)</b>	<b>High (Class III)</b>	<b>Alerts</b>	No alert found	No alert found	<b>Alerts</b>	No alert found	No alert found
Neurontin	marketed	safe	<b>High (Class III)</b>	<b>High (Class III)</b>	No alert found	No alert found	No alert found	<b>Alerts</b>	No alert found	No alert found
Enoxaparin	marketed	safe	<b>High (Class III)</b>	<b>High (Class III)</b>	No alert found	No alert found	No alert found	<b>Alerts</b>	No alert found	No alert found
Lyrica	marketed	safe	Low (Class I)	Low (Class I)	No alert found	No alert found	No alert found	<b>Alerts</b>	No alert found	No alert found

## Reference

- 1) Zakharov, A. V.; Lagunin, A. A.; Filimonov, D. A.; Poroikov, V. V. Quantitative Prediction of Antitarget Interaction Profiles for Chemical Compounds. Chem. Res. Toxicol. 2012, 25 (11), 2378–2385
- 2) QSAR Toolbox (v. 3.3.5), <http://toolbox.oasis-lmc.org/?section=download&version=latest> (accessed Feb 16, 2016)

**Table S2.** Statistical characteristics of binary consensus model (results of 5-fold external cross-validation) compared with QSAR Toolbox

<b>Model</b>	<b>CCR</b>	<b>Sensitivity</b>	<b>PPV</b>	<b>Specificity</b>	<b>NPV</b>	<b>Coverage</b>
<b>Global</b>	0.69	0.72	0.67	0.66	0.70	1.00
<b>Global (AD)</b>	0.74	0.79	0.71	0.69	0.77	0.95
<b>Acylation</b>	0.76	0.65	0.69	0.88	0.85	1.00
<b>Acylation (AD)</b>	0.93	0.92	0.85	0.95	0.97	0.86
<b>No Alert</b>	0.67	0.66	0.63	0.68	0.70	1.00
<b>No Alert (AD)</b>	0.77	0.77	0.72	0.76	0.80	0.90

**Table S3.** Comparison of protein binding alerts, global QSAR models, and consensus QSAR models.

<b>Model</b>	<b>CCR</b>	<b>Sensitivity</b>	<b>PPV</b>	<b>Specificity</b>	<b>NPV</b>	<b>Coverage</b>
QSAR Toolbox	0.63	0.69	0.46	0.57	0.78	1.00
Global QSAR	0.74	0.79	0.71	0.69	0.77	0.95
Consensus QSAR	0.72	0.64	0.71	0.81	0.75	1.00