PASS: Prediction of Activity Spectra for Substances

Twenty Years of Development

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http://www.way2drug.com/passonline
Acknowledgements to the key persons

Dmitry Filimonov, Ph.D.

Tatyana Gloriozova, M.Sc.

Alexey Lagunin, Dr. Sci.

and to many other colleagues who help us in PASS development

Funding: EU FP6 grant No. LSHB-CT-2007-037590, RFBR grants No. 12-04-91445-NIH_a/RUB1-31081-MO-12, 12-07-00597_a and 13-04-91455-NIH_a.
<table>
<thead>
<tr>
<th>ACS Natl. Meetings</th>
<th>Titles of our Presentations</th>
</tr>
</thead>
<tbody>
<tr>
<td>245th (2013)</td>
<td>Virtual high-throughput screening of novel pharmacological agents based on PASS predictions</td>
</tr>
<tr>
<td>239th (2010)</td>
<td>Fragment-based drug design using PASS approach</td>
</tr>
<tr>
<td>237th (2009)</td>
<td>Public molecular databases: How can their value be increased by generation of additional data <em>in silico</em></td>
</tr>
<tr>
<td>235th (2008)</td>
<td>RoadMap data: New possibilities for computer-aided drug discovery</td>
</tr>
<tr>
<td>229th (2005)</td>
<td>Why relevant chemical information cannot be exchanged without disclosing structures</td>
</tr>
<tr>
<td>225th (2003)</td>
<td>Computer-aided discovery of compounds with combined mechanism of pharmacological action in large chemical databases</td>
</tr>
<tr>
<td>222th (2001)</td>
<td>Computer-assisted mechanism-of-action analysis of large databases, including 250,000 chemical compounds registered by NCI</td>
</tr>
</tbody>
</table>
We are living in the time of Big biomedical and chemical Data

Potential biomarkers and pharmacological targets

- 23 chromosomes
- \( \approx 20-25 \) thousand genes
- \( \approx 2 \) mln proteins
- \( \approx 650 \) thousand PPI

Potential chemical probes and pharmaceutical substances

- \( \approx 12-15 \) thousand drug substances
- \( \approx 1,5 \) mln biologically active substances
- \( \approx 60 \) mln commercially available chemical samples
- \( \approx 166 \) biln structures generated \textit{in silico} \(^2\)
- \( \approx 10^{120} \) theoretically possible structures \(^3\)

Most of pharmaceutical substances exhibit pleiotropic effects, which may become the reason:

*E.g.*, *Acetaminophen*

- a) For treatment of certain pathology due to the desirable actions.
- b) For adverse/toxic actions caused severe disorders or even death.

Antipyretic
Analgesic
NSAID
Antiosteoporotic
Antineoplastic
COX inhibitor...

Hepatotoxic...

\[ 	ext{H}_3\text{C}-\text{CON}[\text{aryl}]-\text{OH} \]
To estimate the biological potential of the compound in silico, we proposed the concept of biological activity spectrum:

Biological Activity Spectrum is the intrinsic property of the compound reflected all biological activities, which can be found in the compound’s interaction with biological entity.


Non-synonymous definitions found in literature


Requirements to the creating such program

- Predicts many (ideally, all known) activities
- Uses only structural formula as input data (MOL or SDF)
- Can be re-trained with new data sets
- Has user-friendly interface (“one click” to get prediction)
PASS is based on the ligand-based drug design approach

Full text publications, databases, presentations at conferences etc.

Reliable data on structure and activity of drug-like molecules

PASS Training Set

MNA Descriptors

Training procedure

Bayesian algorithm

New Molecule

PASS SAR Models

Prediction Results
PASS training set is regularly updated and growing

Ca. 1 mln compnds in the training set

Virtual screening of ca. 24 mln compnds

The first presentation (EuroQSAR 1994)

The first Licensee (Merck KGaA)

Virtual screening of ca. 250,000 compnds

Virtual screening of ca. 24 mln compnds

The first publication in English

The first publication

Number of Substances

Number of Predictable Activities

Substances: 959,801
Descriptors: 96,594
Activity Types: 9,596
Selected Activity Types: 7,158
Average IEP: 5.386, %
Prediction:
## PASS 2014 Characteristics

<table>
<thead>
<tr>
<th>Training Set</th>
<th>959,801 drugs, drug-candidates, pharmacological and toxic substances comprise the training set</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological Activity</td>
<td>7,158 biological activities can be predicted (Active vs. Inactive)</td>
</tr>
<tr>
<td>Chemical Structure</td>
<td>Multilevel Neighborhoods of Atoms (MNA) descriptors [1, 2]</td>
</tr>
<tr>
<td>Mathematical Algorithm</td>
<td>Bayesian approach was selected by comparison of many different methods [2]</td>
</tr>
<tr>
<td>Validation</td>
<td>Average accuracy of prediction in LOO CV for the whole training set is ~95% [2]; robustness was shown using principal compounds from MDDR database [3]</td>
</tr>
</tbody>
</table>

Types of biological activity predicted by PASS

- **Main pharmacological effects**
  (antihypertensive, hepatoprotective, anti-inflammatory etc.);

- **Mechanisms of action**
  (5-HT1A agonist, cyclooxygenase 1 inhibitor, adenosine uptake inhibitor, etc.);

- **Specific toxicities**
  (mutagenicity, carcinogenicity, teratogenicity, etc.);

- **Interaction with Antitargets**
  (HERG channel blocker, etc.);

- **Metabolic terms**
  (CYP1A substrate, CYP3A4 inhibitor, CYP2C9 inducer, etc.);

- **Influence on gene expression**
  (APOA1 expression enhancer, NOS2 expression inhibitor, etc.);

- **Action on transporters**
  (Dopamine transporter antagonist, Sodium/bile acid cotransporter inhibitor, etc.).
Results of PASS Prediction for Clopidogrel

45 of 464 Possible Pharmacological Effects at Pa > Pi
0.961 0.004 Neuroprotector
0.896 0.005 Acute neurologic disorders treatment

0.723 0.006 Antithrombotic
0.712 0.004 Platelet aggregation inhibitor
0.618 0.019 Antianginal
0.553 0.013 Atherosclerosis treatment
0.463 0.048 Analgesic
0.385 0.009 Platelet antagonist
0.361 0.027 Stroke treatment
0.352 0.026 Angiogenesis stimulant
0.332 0.017 Anticoagulant
0.366 0.083 Diabetic neuropathy treatment
0.292 0.013 Analgesic, opioid
0.324 0.049 Antiinflammatory, ophthalmic
0.341 0.116 Spasmolytic, urinary
0.290 0.102 Cell adhesion molecule inhibitor
0.301 0.135 Neurodegenerative diseases treatment
0.261 0.098 Antipsoriatic
0.167 0.005 Acetylcholine release stimulant
0.199 0.057 Fibromyalgia syndrome treatment
0.236 0.104 Age-related macular degeneration treatment
0.202 0.075 Pancreatic disorders treatment
0.228 0.104 Amyotrophic lateral sclerosis treatment
0.375 0.254 Vasodilator, cerebral
0.176 0.058 Lipoprotein disorders treatment
0.156 0.047 Diabetic retinopathy treatment
0.257 0.150 Psychotropic

42 Substructure Descriptors; 0 new.
246 of 6400 Possible Activities
45 of 464 Possible Pharmacological Effects
79 of 3850 Possible Mechanisms of Action
108 of 321 Possible Toxic and Adverse Effects
5 of 118 Possible Antitargets
12 of 195 Possible Metabolism-Related Actions
17 of 1610 Possible Gene Expression Regulation
4 of 68 Possible Transporters-Related Actions
Results of PASS Prediction for Clopidogrel

Abdominal pain
Acute neurologic disorders
treatment
Agranulocytosis
Allergic reaction
Anaphylaxis
Anemia
Angioedema
Angiogenesis inhibitor
Antianginal
Antiarthritic
Anticoagulant
Antineoplastic
Antipsoriatic
Antithrombotic
Anxiety
Arthralgia
Atherosclerosis treatment
Back pain
Behavioral disturbance
Blindness
Bronchoconstrictor
Cardioxic
Cataract
CCL4 expression enhancer
CCL5 expression enhancer
Chest pain
Colic
Colitis
Conjunctivitis
Consciousness alteration
Constipation
Cough
CYP2 substrate
CYP2C substrate
CYP2C19 inhibitor
CYP2C19 substrate
CYP2C9 inhibitor
CYP3A substrate
CYP3A4 substrate
Cytochrome P450 inhibitor
Dermatitis
Dermatologic
Dizziness
Drug eruption
Dyspepsia
Emetic
Eosinophilia
Erythema
Erythema multiforme
Exantheme
Flatulence
GP IIb/IIIa receptor antagonist
Hematoxic
Hepatic failure
Hepatitis
Hepatotoxic
Hypertensive
Hyperthermic
Hypotension
Infection
Insomnia
Lassitude
Leukopenia
Lichen planus
Lichenoid eruption
Malaise
Menstruation disturbance
Myalgia
Nausea
Necrosis
Nephrotoxic
Neuroprotector
Neutropenia
Ocular toxicity
Pain
Pancreatitis
Pancytopenia
Platelet aggregation inhibitor
Platelet antagonist
Pruritus
Purpura
Pulmonary embolism

Blue – predictions coincided with the experiment.
Black – unpredictable activities.  Red – unpredicted activities.
Distributions of Pa and Pi for Antineoplastic activity as functions of initial Bayesian estimates
Some publications, where PASS algorithm was described


Examples of PASS-based search for new biologically active compounds
PharmaExpert: Tool for analysis of PASS prediction results
The search for new compounds with multiple mechanisms of action

The search for new compounds with specific therapeutic effect(s) or/and interaction with specific target(s).

Drug repositioning
- *J. Med. Chem., 2004, 47(11), 2870-2876*
- *Pharmaceut. Chem. J., 2011, 45 (10), 605-611*

Assessment of drug-drug interactions and between natural compounds - components of medicinal plants.

- *Curr. Pharm. Des. 2010, 16(15), 1703-1717*
- *Cardiovascul. Therap. Prof., 2008, 7(5), 100-104*
Search for multitargeted compounds using PharmaExpert

Antihypertensive agents, ACE and NEP inhibitors

Antiinflammatory agents, COX-1, COX-2, LOX inhibitors

<table>
<thead>
<tr>
<th>compd</th>
<th>CPE%</th>
<th>COX-1</th>
<th>COX-2</th>
<th>LOX</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57.3 ± 3.4</td>
<td>62.0</td>
<td>0.0</td>
<td>44.0</td>
</tr>
<tr>
<td>2</td>
<td>72.7 ± 6.8</td>
<td>25.0</td>
<td>6.2</td>
<td>51.0</td>
</tr>
<tr>
<td>3</td>
<td>51.1 ± 4.2</td>
<td>8.0</td>
<td>2.5</td>
<td>22.4</td>
</tr>
<tr>
<td>4</td>
<td>66.1 ± 1.2</td>
<td>60.0</td>
<td>4.5</td>
<td>12.5</td>
</tr>
<tr>
<td>5</td>
<td>69.4 ± 2.3</td>
<td>25.0</td>
<td>12.1</td>
<td>76.0</td>
</tr>
<tr>
<td>6</td>
<td>54.2 ± 2.4</td>
<td>31.0</td>
<td>6.2</td>
<td>25.0</td>
</tr>
<tr>
<td>7</td>
<td>44.5 ± 1.8</td>
<td>90.0</td>
<td>30.4</td>
<td>12.0</td>
</tr>
<tr>
<td>8</td>
<td>62.0 ± 2.5</td>
<td>50.0</td>
<td>2.1</td>
<td>44.2</td>
</tr>
<tr>
<td>9</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Computer-Aided Selection of Potential Antihypertensive Compounds with Dual Mechanism of Action

Alexey A. Lagunin, Oleg A. Gomazov, Dmitrii A. Filimonov, Tatyana A. Goreeva, Elvira A. Dilakyan, Elena V. Kugaevskaya, Yulia E. Eliseeva, Nina I. Solovyeva, and Vladimir V. Poraiko

Institute of Biomedical Chemistry of Russian Academy of Medical Sciences, Pogodinsky St, 10, Moscow 119121, Russia
Received November 8, 2002

The prediction of biological activity spectra for substances as an approach for searching compounds with complex mechanisms of action was studied. New compounds with dual mechanisms of antihypertensive action were found by this approach. Biological activity spectra for substances were predicted on the basis of their structural formulas by the computer program PASS. Thirty molecular mechanisms of action of compounds from the MDDR 99.2 database, which cause the antihypertensive effect and can be predicted by PASS, were identified. The analysis of predictions for compounds with 15 dual antihypertensive mechanisms of action from the MDDR 99.2 database has confirmed high accuracy of prediction. This approach was applied to databases of commercially available compounds (AssistedChemBridge) and allowed us to select four substances that are potential inhibitors of angiotensin converting enzyme (ACE) and neutral endopeptidase (NEP). At a later time, all these compounds were found to be the inhibitors of both ACE and NEP. The most potent compounds had IC_{50} of 10^{-9} - 10^{-8} M for ACE and 10^{-7} - 10^{-6} M for NEP. New combinations of dual mechanisms of action never before found for antihypertensive compounds were predicted.

Computer-Aided Discovery of Anti-Inflammatory Thiazolidinones with Dual Cyclooxygenase/Lipoxygenase Inhibition


Department of Pharmaceutical Chemistry, School of Pharmacy, Aristotle University, Thessaloniki, 54124, Greece, Institute of Biomedical Chemistry of Russian Academy of Medical Sciences, Pogodinsky St, 10, Moscow, 119221, Russia, and Medicinal Chemistry Division, Central Drug Research Institute, Chatar Maiel Palace, Lucknow-226 003, India
Received July 24, 2007

New anti-inflammatory agents possessing dual cyclooxygenase/lipoxygenase (COX/LOX) inhibition were discovered by computer-aided prediction of biological activity for 573 virtually designed chemical compounds. Prediction of biological activity was performed by PASS, and prediction results were analyzed with PharmaExpert software. Nine 2-(thiazole-2-yl)-5-phenoxyethane-4-thiazolidinone derivatives differing by the phenyl group substitution were selected for synthesis and experimental testing as potential COX/LOX inhibitors. Eight tested compounds exhibited anti-inflammatory activity in the carrageenin-induced paw edema. It was shown that seven tested compounds (77.8%) were COX inhibitors, seven compounds were COX inhibitors (77.8%), and six tested compounds (66.7%) were dual COX/LOX inhibitors. Analysis of lipophilicity of the compounds showed a negative correlation with inhibition of edema formation. The binding modes of the most active compounds of this series (2-(thiazole-2-yl)-5-(m-nitrophenyl)ethane-4-thiazolidinone for COX-1 and COX-2, and 2-(thiazole-2-yl)-5-(m-nitrophenyl)ethane-4-thiazolidinone for 15-LOX) were proposed on the basis of docking studies.
Finding of nootropic effect in some antihypertensive drugs based on PASS prediction

<table>
<thead>
<tr>
<th>Name</th>
<th>Pa (Nootropic effect), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>44,6</td>
</tr>
<tr>
<td>Enalapril</td>
<td>65,5</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>61,8</td>
</tr>
<tr>
<td>Perindopril</td>
<td>60,9</td>
</tr>
<tr>
<td>Quinapril</td>
<td>65,1</td>
</tr>
<tr>
<td>Ramipril</td>
<td>63,3</td>
</tr>
<tr>
<td>Monopril</td>
<td>30,9</td>
</tr>
<tr>
<td><strong>Piracetam</strong></td>
<td><strong>81,7</strong></td>
</tr>
<tr>
<td>Amlodipin</td>
<td>-</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>-</td>
</tr>
</tbody>
</table>

Perindopril in dose of 1 mg/kg, and quinapril and monopril in doses of 10 mg/kg improved the patrolling behavior in the maze, like piracetam and meclofenoxate (in doses of 300 and 120 mg/kg, respectively).

Participants: 9 teams from 8 countries

European project «From analysis of gene regulatory networks to drug» (Net2Drug)

ChemNavigator database (~24,000,000 structures of organic compounds)

Virtual screening of potential multitarget anticancer substances (PASS, GUSAR)

11 compounds tested in cellular assays

Further progress:
Activity confirmed in experiments on mouse xenograft models

ALab – resident of «Skolkovo» (2012)
Grant of «Skolkovo» (2013)
More active analogs (2014)

2 active compounds (BC, melanoma)
Synergism with RITA.
Get more information about biological potential of your compounds.

PASS Online predicts over 4000 kinds of biological activity, including pharmacological effects, mechanisms of action, toxic and adverse effects, interaction with metabolic enzymes and transporters, influence on gene expression, etc.

To obtain the predicted biological activity profile for your compound, only structural formula is necessary; thus, prediction is possible even for virtual structure designed in computer but not synthesized yet.

Accessing to PASS Online service requires a prior registration, which is free but one should agree with the Terms & Conditions for usage of this service.

http://way2drug.com/passonline
Prediction for structure presented by MOL file
### Prediction Results

![PASS Online](image)

**Predict new compound**
**View old results**
**View/change profile**

- **SMILES**
- **MOL file**
- **Marvin applet**

**F:\DATABASE\TEST-MOLEC**

[Get prediction]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prorenoconstrictor</td>
<td>0.14</td>
</tr>
<tr>
<td>Platelet aggregation inhibitor</td>
<td>0.712</td>
</tr>
<tr>
<td>Pain</td>
<td>0.733</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0.719</td>
</tr>
<tr>
<td>Cataract</td>
<td>0.698</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>0.718</td>
</tr>
<tr>
<td>Consciousness alteration</td>
<td>0.703</td>
</tr>
<tr>
<td>Lactic</td>
<td>0.700</td>
</tr>
<tr>
<td>Headache</td>
<td>0.697</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>0.682</td>
</tr>
<tr>
<td>CYP2C19 inhibitor</td>
<td>0.650</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.659</td>
</tr>
</tbody>
</table>
PASS Online Utilization in 2013

Total number of registered users: >10,000
Total number of countries: >90
Total number of predictions: >300,000
Over 150 independent publications with PASS online predictions (>50% papers with experimental testing of prediction results)
Example 1. Virtual screening of the synthetic library

2648 organic molecules

PASS Predictions
Xanthine oxidase inhibitors

32 hits; 24 tested

IC$_{50}$ = 9.4 uM

IC$_{50}$ = 30.2 uM

IC$_{50}$ = 1.4 uM

Reference drug
Allopurinol
IC$_{50}$ = 5.7 uM

Example 2. Prediction of the most probable activities of xantones and thioxantones for testing *in vitro*

The only activities that were tested are antimicrobial (*S. aureus, S. pneumonia, S. pyogenes, M. catarrghalis, H. influenza, E. Coli*) and cyrotoxic (*HepG2 and Jurkat cell lines*). *No such activities were predicted and found experimentally*.


<table>
<thead>
<tr>
<th>Activity</th>
<th>Pa</th>
<th>Pi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antineurotoxic</td>
<td>0.859</td>
<td>0.005</td>
</tr>
<tr>
<td>Insulin and Insulin analogs</td>
<td>0.781</td>
<td>0.004</td>
</tr>
<tr>
<td>Fibrinolytics</td>
<td>0.776</td>
<td>0.009</td>
</tr>
<tr>
<td>Antihelmintic (Nematodes)</td>
<td>0.629</td>
<td>0.009</td>
</tr>
<tr>
<td>Postmenopausal disorders treatment</td>
<td>0.625</td>
<td>0.003</td>
</tr>
<tr>
<td>Antidote, cyanide</td>
<td>0.541</td>
<td>0.008</td>
</tr>
<tr>
<td>Keratolytic</td>
<td>0.536</td>
<td>0.005</td>
</tr>
<tr>
<td>Antihelmintic</td>
<td>0.512</td>
<td>0.005</td>
</tr>
<tr>
<td>Thioredoxin inhibitor</td>
<td>0.705</td>
<td>0.009</td>
</tr>
<tr>
<td>Phosphatidylinositol 3-kinase gamma inhibitor</td>
<td>0.553</td>
<td>0.005</td>
</tr>
<tr>
<td>Quercetin 2,3-dioxygenase inhibitor</td>
<td>0.543</td>
<td>0.005</td>
</tr>
<tr>
<td>Thioredoxin disulfide reductase inhibitor</td>
<td>0.541</td>
<td>0.007</td>
</tr>
<tr>
<td>FMO3 substrate</td>
<td>0.540</td>
<td>0.008</td>
</tr>
<tr>
<td>CF transmembrane conductance regulator inhibitor</td>
<td>0.539</td>
<td>0.005</td>
</tr>
<tr>
<td>Sulfotransferase substrate</td>
<td>0.505</td>
<td>0.004</td>
</tr>
<tr>
<td>Estrogen beta receptor agonist</td>
<td>0.501</td>
<td>0.001</td>
</tr>
</tbody>
</table>
Example 3. Prediction of the most probable activities of pyranopyrazole derivatives for testing *in vivo*

Analgesic and anti-inflammatory activity of these compounds was shown on experimental models in mice. Using docking the authors concluded that COX-2 inhibiting activity reduces in the following order: phenothiazolyl > benzothiazolyl > quinolyl > pyridiminyln > OCH₃ > Br > CH₃ > H. However, these conclusions require experimental verification.


<table>
<thead>
<tr>
<th>Activity</th>
<th>Pa</th>
<th>Pi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesic, non-opioid</td>
<td>0</td>
<td>0.702</td>
</tr>
<tr>
<td>5-hydroxytryptamine release</td>
<td>0</td>
<td>0.005</td>
</tr>
<tr>
<td>Antineoplastic (Ovarian Cancer)</td>
<td>0</td>
<td>0.677</td>
</tr>
<tr>
<td>Analgesic</td>
<td>0</td>
<td>0.621</td>
</tr>
<tr>
<td>Antiarthritic</td>
<td>0</td>
<td>0.606</td>
</tr>
<tr>
<td>Cognition disorders</td>
<td>0</td>
<td>0.597</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>0</td>
<td>0.592</td>
</tr>
<tr>
<td>Antiviral (Arbovirus)</td>
<td>0</td>
<td>0.613</td>
</tr>
<tr>
<td>Complement factor D inhibitor</td>
<td>0</td>
<td>0.572</td>
</tr>
<tr>
<td>Immunomodulator</td>
<td>0</td>
<td>0.532</td>
</tr>
<tr>
<td>Immunosuppressant</td>
<td>0</td>
<td>0.454</td>
</tr>
<tr>
<td>Cyclooxygenase inhibitor</td>
<td>0</td>
<td>0.400</td>
</tr>
<tr>
<td>HCV IRES inhibitor</td>
<td>0</td>
<td>0.431</td>
</tr>
</tbody>
</table>
Systematic review of these >150 publications is accepted for publication by “Chemistry of Heterocyclic Compounds”

**Graphical abstract**

D. A. Filimonov, A. A. Lagunin, T. A. Gloriozova, A. V. Rudik, D. S. Druzhilovsky, P. V. Pogodin, V. V. Poroikov
Prediction of biological activity of organic compounds using web-resource PASS Online

<table>
<thead>
<tr>
<th>Pa</th>
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<th>Activity</th>
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<tr>
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<tr>
<td>0.776</td>
<td>0.009</td>
<td>Fibrinolytics</td>
</tr>
</tbody>
</table>

In December 2013 we executed an interview of active PASS Online users.

Please fill in the Anonymous form below.

1. Where are you working?
   - Academy (University)
   - Research Institute
   - Industry
   - Regulatory Agency
   - Other (Please, specify)

2. What is your field of activity?
   - Organic Chemistry
   - Medical Chemistry
   - Pharmacology
   - Toxicology
   - Pharmacy
   - Other (Please, specify)

3. What is your primary aim to use PASS Online service?
   - Planning of Chemical Synthesis
   - Planning of Biological Testing
   - Finding new Actions of Known compounds
   - Chemical Safety & Risk Assessment
   - Other (Please, specify)

4. How satisfied are you by PASS Online service?
   - Very Satisfied
   - Satisfied
   - Neutral
   - Dissatisfied
   - Very Dissatisfied
   On PASS Online service how I feel about...
   - Registration procedure
   - Structure input
   - Accessibility via internet
   - User interface
   - Speed of response
   - List of predicative activities
   - Results of prediction

5. To improve PASS Online service are you ready...
   - Very Likely
   - Unlikely
   - Likely
   - Unlikely
   - Very Likely
   I am ready...
   - To submit feedback about correspondence of predictions with the experiment
   - To submit the proposal what can be done for improvement of PASS Online
   - To submit the proposal which biological activity should be covered by PASS Online
   - To submit the proposal which chemical series should be covered by PASS Online
   - To take part in the joint work to input data on active compounds from particular chemical series to update PASS Online training set
   - To refer on PASS Online prediction results in my publications
   - To recommend PASS Online service to other colleagues

6. Are you willing to share some information about your activity, to find some partners for collaborative projects?
   - Very Likely
   - Likely
   - Likely
   - Unlikely
   - Very Unlikely
   - I am willing...
   - To share some information about my activity
   - To find some partners for collaborative projects

Note: The form contains questions and options for responses, but specific text is not provided for each question.
Where are you working?

Academy (University) - 130
Research Institute - 20
Other - 10

Primary aim to use PASS Online

Planning of Biological Testing - 120
Planning of Chemical Synthesis - 110
Finding New Actions of Known Compounds - 100
Chemical Safety & Risk Assessment - 80
Other - 5

Field of activity

Medicinal Chemistry - 120
Organic Chemistry - 100
Pharmacology - 90
Pharmacy - 50
Toxicology - 40
Other - 20
Most of users are ready:

• To inform us about the experimental results
• To make suggestions how web-resource can be improved
• To add new information to the training set
• Refer in publications
• Recommend to colleagues
• Try to obtain joint grants
Major comments of the users

1. Acknowledgements etc.
2. Collaboration
3. Interface, general remarks
4. Presentation of the prediction results
5. Input of data
6. Training set
7. List of activities
8. Miscellaneous
1. PASS provides information about most probable biological activities based on structural formulae of organic compounds.

2. PASS predictions can be used for planning of synthesis and biological testing.

3. PASS Online is widely used by organic and medicinal chemists, pharmacologists etc.

4. Recommendations of PASS Online users provided during the interview can be used for further improvement of the web-resource.

5. PASS Online web-resource may become a platform for many collaborative projects in the field of drug discovery.
Thanks for your kind attention!

Visit our web-page:
www.way2drug.com/passonline

Your questions, pls., address to:
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20th EuroQSAR
Understanding Chemical-Biological Interactions

20-th European Symposium on Quantitative Structure-Activity Relationships

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