# Supporting Information

**Evaluating the mutagenic potential of aerosol organic compounds using informatics based screening**

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**Number of tables: 10 (5 of which provided in full extent as attached Excel files)**

**Number of figures: 2**

## **Table S1**. List of the 104 organic compounds for QSAR analysis. (provided as an attached Excel file)

## **Table S2.** OECD QSAR Toolbox description and Profilers for genotoxicity.

| Tool | Information | |
| --- | --- | --- |
| OECD QSAR Toolbox | The OECD QSAR Toolbox (version 3.3, 2015) is a software application developed by the Organization for Economic Cooperation and Development (OECD) to use (Q)SAR methodologies to group chemicals into categories and to fill data gaps by read-across and trend analysis. The OECD (Q)SAR Application Toolbox is intended to be used by governments, chemical industry and other stakeholders in filling gaps in (eco)toxicity data needed for assessing the hazards of chemicals. It is currently recommended and released by the European Chemicals Agency (ECHA) in collaboration with OECD. The Toolbox incorporates information and tools from various sources into a logical workflow. Crucial to this workflow is grouping chemicals into chemical categories. The seminal features of the Toolbox are the identification of relevant structural characteristics and potential mechanism or mode of action of a target compound, the identification of other chemicals that have the same structural characteristics and/or mechanism or mode of action and the use of existing experimental data to fill the data gap(s) . | |
| Toolbox Profiler | **Information** | **Descriptor type** |
| DNA binding by OASIS v.1.3 | It was developed from an analysis of Ames mutagenicity data. The structural alerts within this profiler are detailed by Mekenyan et al. (2004) and Serafimova et al. (2007). The profiler was based on the 78 structural alerts responsible for interaction with DNA analyzed in Ames Mutagenicity model. The scope of the profiler is to investigate presence of alerts within target molecules responsible for interaction with DNA. The list of 78 structural alerts has been separated into seven mechanistic domains. Each of the mechanistic domains has been separated into more than 12 mechanistic alerts. The profiling result outcome assigns a target to the corresponding structural alert, mechanistic alerts and domain. | Mechanistic profile |
| DNA binding by OECD | It was developed and donated to the OECD QSAR Toolbox by Dr Enoch and Prof. Cronin form Liverpool John Moores University, UK. It compiles mechanistic organic chemistry fragments (in the form of structural alerts) for the binding of organic chemicals to DNA. The profiler was created following the mapping of existing structural alerts for mutagenicity and carcinogenicity. The mapping was performed to achieve maximum overlap and usability whilst restricting redundancy in the alerts, and to ensure that the alerts related to the molecular initiating event of covalent DNA binding by OECD. It includes a total of 60 new or re-defined alerts across six broad organic chemistry mechanisms and it represents the most comprehensive listing of structural alerts for DNA binding by OECD currently available. | Mechanistic profile |
| DNA alerts for AMES, MN and CA by OASIS v.1.3 | It includes categories or chemical mechanism of DNA binding particularly relevant for genotoxic endpoints. | Mechanistic profile |
| *in vitro* mutagenicity (Ames test) alerts by ISS | It is based on the Mutagenicity/Carcinogenicity module of the software Toxtree. It works as a decision tree for estimating in vitro (Ames test) mutagenicity, based on a list of 30 structural alerts (SAs). The SAs for mutagenicity are molecular functional groups or substructures known to be linked to the mutagenic activity of chemicals. As one or more SAs embedded in a molecular structure are recognised, the system flags the potential mutagenicity of the chemical. The present list of SAs is a subset of the original Toxtree list, obtained by eliminating the SAs for nongenotoxic carcinogenicity. | Structural alert |
| *in vivo* mutagenicity (Micronucleus) alerts by ISS | It is based on the ToxMic rulebase of the software Toxtree. This rulebase provides a list of 35 structural alerts (SAs) for a preliminary screening of potentially in vivo mutagens. These SAs are molecular functional groups or substructures that are known to be linked to the induction of effects in the in vivo micronucleus assay. The compilation of SAs for the in vivo micronucleus assay in rodents is based on both the existing knowledge on the mechanisms of toxic action and on a structural analysis of the chemicals tested in the assay. | Structural alert |

## **Table S3.** Public databases for genotoxicity and carcinogenicity.

| Database | Information |
| --- | --- |
| Bacterial mutagenicity ISSSTY | Istituto Superiore di Sanità (ISS) ISSSTY database on *Salmonella typhimurium* (Ames test) bacterial mutagenicity. The experimental results were retrieved from the Chemical Carcinogenesis Research Information System (CCRIS) database, in the Toxnet databases cluster (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS). |
| Carcinogenic potency database (CPDB) | The Carcinogenic Potency Database (CPDB) (http://potency.berkeley.edu/cpdb.html) provides a unique resource of the results of 6540 chronic, long-term animal cancer tests on 1547 chemicals. The CPDB provides easy access to the bioassay literature, with qualitative and quantitative analyses of both positive and negative experiments that have been published over the past 50 years in the general literature through 2001 and by the National Cancer Institute/National Toxicology Program through 2004. |
| Carcinogenicity & Mutagenicity ISSCAN | This database, developed by the Istituto Superiore di Sanità (ISS, Rome, Italy), contains information on more than 1150 chemical compounds tested with the long-term carcinogenicity bioassay on rodents (rat, mouse). Historically, this database was developed to support the development of (Q)SAR models for chemical carcinogenicity. ISSCAN is downloadable in pdf, xls and sdf formats, and is searchable by chemical name and CAS number. |
| ECHA CHEM | ECHA CHEM includes information on chemical substances manufactured or imported in Europe. The information originates from the registration dossiers, submitted by companies to the European Chemicals Agency (ECHA) in the framework of the REACH Regulation (http://echa.europa.eu/chem\_data\_en.asp). |
| Genotoxicity OASIS | Genotoxicity OASIS includes experimental results for genotoxicity for 7500 compounds collected from several sources, e.g. Hansen et al (2009)[[1]](#footnote-1), CPDB + NTP + IARC (International Agency for Research on Cancer - Monographs on the evaluation of carcinogenic risks to humans)[[2]](#footnote-2),[[3]](#footnote-3), LSIC Japan-Danish EPA Inventory, NCI-STTP (Short-Term Testing Program in the National Cancer Institute (NCI), National Institutes of Health, US Department of Health and Human Services), NTP Program - P&G Inventory and US GeneTox. It contains data for mutagenic valuation by Ames test (*Salmonella Typhimurium*, strains TA 97, TA 98, TA 100, TA 1535, TA 1537, TA 1538) with and without metabolic activation (liver S9 enzyme fraction). It also includes data for chromosomal aberrations determined by *in vitro* test using Chinese hamster lung cells (CHL, with and without S9). Micronucleus (MN) and mouse lymphoma gene mutation assay (MLA) are evaluated by Chinese hamster lung cells (CHL/IU) and by in vitro T-lymphoma cell lines, respectively. All endpoints are evaluated in dichotomic scale (YES/NO). |
| Toxicology Data Network Database (TOXNET) | The TOXNET database of the US National Library of Medicine (NLM) is a cluster of different databases, collecting information on toxicology, hazardous chemicals, environmental health, and toxic releases. Among the TOXNET databases, the **Chemical Carcinogenesis Research Information System (CCRIS)** and the **GENE-TOX** databases deal specifically with mutagenicity and carcinogenicity data. CCRIS contains over 9000 chemical records with animal carcinogenicity, mutagenicity, tumour promotion, and tumor inhibition test results provided by the National Cancer Institute (NCI). Test results have been reviewed by experts in carcinogenesis and mutagenesis. GENE-TOX was developed by the US EPA and contains genetic toxicology (mutagenicity) test data, resulting from expert peer review of the open scientific literature, on over 3000 chemicals. |
| Toxicity Japan MHLW (EXCHEM) | This database (http://dra4.nihs.go.jp/mhlw\_data/jsp/SearchPageENG.jsp) was developed by the Chemicals Investigation Promoting Council, Japan and was supervised by Office of Chemicals Safety Evaluation and Licensing Bureau Pharmaceutical and Food Safety Bureau Ministry of Health, Labour and Welfare (MHLW), Japan. EXCHEM contains data for Ames mutagenicity, chromosomal aberrations and mouse micronucleus assays for more than 250 HPV chemicals. Most of the information is in Japanese but there is also information in English. The database is searchable by CAS number and name. |

## Table S4. Employed tools for genotoxicity prediction.

|  | **ACD/Impurity Profiling (Salmonella composite model)** | **Vega/CAESAR Mutagenicity model** |
| --- | --- | --- |
| **Background Information** | ACD/Percepta Package for Toxicity Screening of Impurities (ACD/Impurity Profiling) provides a battery of *in silico* models to accurately assess the genotoxic and carcinogenic potential of chemicals. The impurity profiling module is a result of the collaboration between ACD/Labs and FDA Center for Food Safety and Nutrition (CFSAN). This module includes probabilistic predictive models for 21 different endpoints that cover various mechanisms of hazardous activity (including Mutagenicity, Clastogenicity, DNA damage mechanisms, Carcinogenicity and Endocrine Disruption mechanisms), and that are based on experimental data obtained from FDA. | Vega (Virtual Models for evaluating the properties of chemicals within a global architecture, version 1.1.1, 2015 - VegaNIC application, Laboratory of Environmental Chemistry and Toxicology of Mario Negri Institute of Pharmacological Research) is a platform developed based on contributions from the EU projects CAESAR, ORCHESTRA and ANTARES. Vega Mutagenicity model includes CAESAR QSAR model for mutagenicity. |
| **Availability** | Commercial | Free |
| **Dataset** | 7826 compounds (49.5% positive) | 3253 compounds |
| **Modelling algorithm** | Probabilistic predictive models were developed using GALAS modelling methodology. Each GALAS model consists of two parts: 1) a global (baseline) model, built using binomial PLS method based on fragmental descriptors, that reflects a “cumulative” mutagenicity potential; 2) local corrections are applied to baseline predictions using a special similarity-based routine, after performing an analysis for the most similar compounds used in the training set. | It is an integrated model made of two complementary techniques: a machine learning algorithm (SVM), to build an early model with the best statistical accuracy, equipped with an expert facility for false negatives removal based on known structural alerts, to refine its predictions. |
| **Outcome** | The probabilistic models provide: the probability that a compound will result in a positive test in the respective assay (“p-value”); an indication of whether the compound belongs to the model applicability domain according to the calculated RI value; a “positive” or “negative” call if the compound can be reliably classified on the basis of p and RI values (“Undefined” otherwise) | The model provides a qualitative prediction of mutagenicity on Salmonella typhimurium (Ames test), information on applicability domain (ADI index), and reasoning on identified fragments and/or structural alerts. |
| **Model Statistics** | Sensitivity = 87.1%, Specificity = 81.7% | Sensitivity = 97%, Specificity = 86% |
| **Prediction Reliability** | Reliability Index (RI): it ranges from 0 to 1, and gives an evaluation of whether a submitted compound falls within the Model Applicability Domain. In particular: RI < 0.3 (Not Reliable), RI in range 0.3-0.5 (Borderline Reliability), RI in range 0.5-0.75 (Moderate Reliability), RI >= 0.75 (High Reliability). Estimation of the RI takes into account the following two aspects: similarity of the tested compound to the training set and the consistency of experimental values for similar compounds. | Applicability Domain Index (ADI): it ranges from 0 to 1, and gives an evaluation of whether a submitted compound falls within the Model Applicability Domain. In particular: ADI > 0.9 means that the predicted substance is into the AD of the model; ADI < 0.7 means that the predicted substance is out of the AD of the model; ADI in range 0.7-0.9 means that the predicted substance could be out of the AD of the model. The ADI is calculated by grouping several other indices, each one taking into account a particular issue of the AD, e.g. similar molecules with known experimental value, concordance for similar molecules, accuracy of prediction for similar molecules, atom Centered Fragments similarity check, model descriptors range check. |
| **Mechanistic Information** | Structural alerts for mutagenicity, clastogenicity, and epigenetic carcinogenicity. | Structural alerts for mutagenicty and suspect mutagenicity. |
| **Structural analogues** | Up to 5 most structurally similar structures from the training set are shown along with experimental results. The structural similarity is evaluated by means of Tanimoto similarity coefficient (calculated using MACCS-II similarity key). | Six most similar compounds found in the training and test set of the model are shown, along with some relevant information (e.g., CAS, experimental and predicted value). The similarity index considers molecule's fingerprint and structural aspects (e.g., count of atoms, rings and relevant fragments). |

## Table S5. List of physico-chemical, structural and mechanistic descriptors. (provided as an attached Excel file)

## Table S6. Experimental Ames test studies retrieved for 13 aerosol compounds (provided as an attached Excel file)

## Table S7. QSAR predictions for Salmonella in vitro mutagenicity generated for 104 aerosol compounds (provided as an attached Excel file)

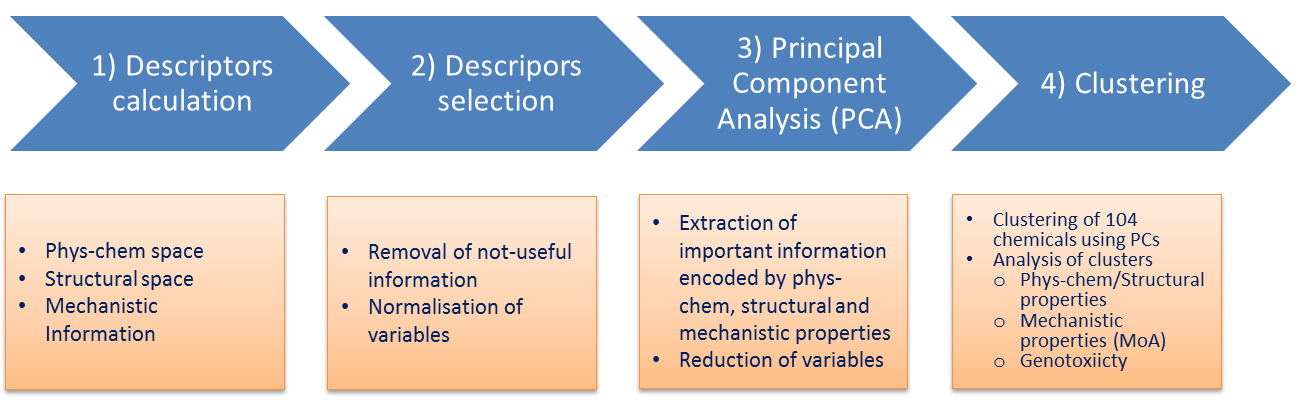
## Table S8a. Composition of the clusters with summarized mechanisms of alert (MoA). An additional table (Table S8b) with the MoA specified for each compounds in the clusters is provided as an attached Excel file.

|  |  |  |  |
| --- | --- | --- | --- |
| Cluster | ID Compounds | N | Cluster assessment |
| 0 | mtr\_10\*, mtr\_11, mtr\_12 | 3 | * Same SOA class: Monoterpene * Same MoAs for genotoxicity * Same alerts: Four- and Five-Membered Lactones, H-acceptor-path3-H-acceptor, Oxolane * Reliable predictions: 2 positive; 1 negative * Remarks/Implications: Further confirmation needed for mtr\_10(\*) negative prediction (e.g., integrate with other *in silico* predictors) |
| 1 | lmp\_02, lmp\_09, lmp\_17\* | 3 | * Same SOA class: low MW PAH * Same MoAs for genotoxicity * Same alerts: Quinones, H-acceptor-path3-H-acceptor, Alpha, beta- unsaturated ketones * All positive genotoxicity predictions * Positive experimental data available for 1 cluster member (Imp 02) * Remarks/Implications: Cluster information increases the confidence of the bordeline reliable prediction of lmp\_17(\*) |
| 2 | ara\_01, ara\_02, ara\_03, ara\_04, ara\_05 | 5 | * Same SOA class: aromatic amine * Same MoAs for genotoxicity * Same alerts: N-Nitroso alert, H-acceptor-path3-H-acceptor * Reliable positive predictions for all cluster members * Positive experimental data available for 3 cluster members * Remarks/Implications: No need for further assessment of Cluster 2 members |
| 3 | dic\_09\*, lmp\_10, lmp\_11, lmp\_20, lmp\_21, lmp\_23 | 6 | * Main SOA class composition: low MW PAH * Different MoAs associated to the following alerts: nitro-aromatic AND/OR polycyclic aromatic hydrocarbons * All positive genotoxicity predictions (except for dic\_09) * Positive experimental data available for 3 cluster members * Remarks/Implications: indeterminate prediction of dic\_09(\*) is not supported by the cluster (different MoAs/alerts), highlighting the need for experimental data for this compound |
| 4 | lmp\_03\*, lmp\_04, lmp\_15\*, lmp\_16\*, lmp\_19# | 5 | * Same SOA class: low MW PAH * Same MoAs for 3 cluster members (\*) * Alerts: alpha, beta-Unsaturated Aldehydes, Simple aldehyde, H-acceptor-path3-H-acceptor * Common alert: aldehyde * Indeterminate predictions for 4 members (\*/#) * Remarks/Implications: 1) Need for experimental data for Imp\_19(#); 2) Need for experimental data for one compound and possible read-across predictions for other compounds (\*) |
| 5 | dic\_02\*, mtr\_04, mtr\_20 | 3 | * Two SOA classes: Monoterpene and Dicarbonyl (C2-C3) * Alerts: Simple aldehyde, H-acceptor-path3-H-acceptor * Common alert: simple aldehyde * Same mechanistic profile for dic 02 and mtr 20 * Negative predictions for 2 members and 1 indeterminate prediction (\*) * Remarks/Implications: Need for experimental data for dic\_02(\*) and possible read-across from dic\_02 to mtr\_20 to support the borderline prediction |
| 6 | mtr\_26, mtr\_27 | 2 | * Same SOA class: Monoterpene * Same MoA for genotoxicity * Common alerts: Organic Peroxy Compounds and H-acceptor-path3-H-acceptor * Reliable negative predictions for both cluster members * Remarks/Implications: No need for further assessment of Cluster 6 members |
| 7 | alb\_05, alb\_09, alb\_12, alb\_13, alb\_14, mtr\_25 | 6 | * Two SOA classes: Alkylbenzene, Monoterpene * Different MoAs for genotoxicity * Common Alerts: H-acceptor-path3-H-acceptor, Carbonyl group, Epoxide and/or Organic Peroxy Compounds * Reliable positive genotoxicity predictions for all cluster members * Remarks/Implications: No need for further assessment of Cluster 7 members |
| 8 | alb\_06, alb\_08, alb\_10, alb\_11\*, alb\_16, ken\_01, ken\_02\*, ken\_03\*, mtr\_03, mtr\_21, mtr\_22\*, mtr\_23, mtr\_24 |  | * Three SOA classes: Alkylbenzene, Monoterpene, Alkenes ozonolysis * Different MoAs for genotoxicity * Alerts: H-acceptor-path3-H-acceptor (all), Peroxy compound (except alb\_16), Carbonyl group (except alb\_10, alb\_11, alb\_08, ken\_01, mtr\_23), Four- and Five-Membered Lactones AND Oxolane (only alb\_10, alb\_11) * Genotoxicity predictions: positive/negative/indeterminate * Remarks/Implications: Need for experimental data for indeterminate predictions (\*) |
| 9\_0 | mtr\_15, mtr\_16 | 2 | * Same SOA class: Monoterpene * Same alert: H-acceptor-path3-H-acceptor * Reliable negative genotoxicity predictions for both cluster members * Remarks/Implications: No need for further assessment of the sub-cluster 9\_0 members |
| 9\_1 | kan\_01, kan\_02, kan\_03, kan\_04, kan\_05, kan\_06 | 6 | * Same SOA class: Alkane photooxidation * No alerts for genotoxicity, exept for kan\_04 and kan\_05 (same alerts: H-acceptor-path3-H-acceptor, Oxolane) * Reliable negative genotoxicity predictions for all cluster members * Remarks/Implications: No need for further assessment of the sub-cluster 9\_1 members |
| 9\_2 | alb\_01, alb\_02, alb\_03, alb\_04, lmp\_01, lmp\_05, lmp\_06, lmp\_07, lmp\_08, lmp\_12#, lmp\_13\*, lmp\_14\*, lmp\_18, lmp\_22 | 14 | * Two SOA classes: low MW PAH and Alkylbenzene * Different MoAs for genotoxicity * Same alerts: H-acceptor-path3-H-acceptor, Alkyl phenols, Nitro-Aromatic group, Hydroquinones, 9,10-dihydrophenanthrenes, Alpha-beta-dicarbonyl * Different genotoxicity predictions: positive/negative/indeterminate * Remarks/Implications: 1) Need for further assessment for lmp\_13 and lmp\_14(\*) (experimental data or possible read-across from Imp\_07 negative data); 2) Further confirmation needed for lmp\_12(#) positive prediction (e.g., integrate with other *in silico* predictors) |
| 9\_3 | alb\_07, alb\_15, alb\_17, alb\_18, dic\_01#, dic\_03\*\*, dic\_04, dic\_05, dic\_06, dic\_07, dic\_08, iso\_01, iso\_02, iso\_03\*\*, iso\_04, iso\_05\*, iso\_06, iso\_07, iso\_08\*\*, mtr\_01\*\*, mtr\_02, mtr\_05, mtr\_06, mtr\_07, mtr\_08\*\*, mtr\_09, mtr\_13, mtr\_14, , mtr\_17, mtr\_18, mtr\_19, mtr\_28, mtr\_29, mtr\_30, mtr\_31, str\_01 | 36 | * Different SOA classes * Different MoAs for genotoxicity * Alerts: H-acceptor-path3-H-acceptor (all – majority are negative), Organic Peroxy Compounds (only mtr\_28, alb\_07 – both positive), Oxolane (only iso\_05 – indeterminate), Specific Acetate Esters (only mtr\_14 – negative) * Different genotoxicity predictions: negative (75%)/positive/indeterminate * Remarks/Implications: Further assessment needed for some cluster members, e.g. 1) Need for experimental data for iso\_05(\*); 2) Further confirmation needed for dic\_01 (#) positive prediction (e.g., integrate with other *in silico* predictors); 3) Need for experimental data for one compound and possible read-across predictions for other compounds (\*\*) |

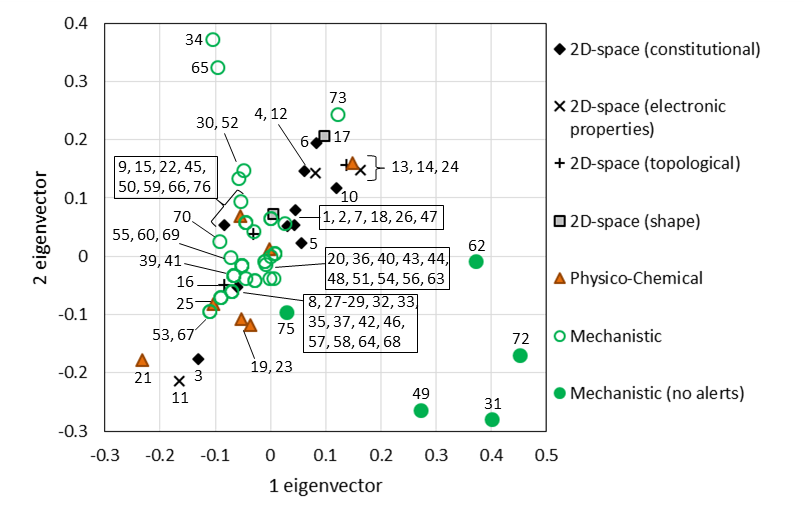
**Table S9.** Distribution of mutagenic (red); non-mutagenic (green) and indeterminate (grey) compounds between clusters and SOA classes.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cluster** | **Isoprene SOA** | **Di-carbonyl SOA** | **Mono-terp SOA** | **Sesqui-terp SOA** | **Alkene SOA** | **Alkane SOA** | **Subst. benzene SOA** | **low MW PAH SOA** | **amine SOA** | **total** |
| 0 |  |  | **2 + 1** |  |  |  |  |  |  | **3 (2 + 1)** |
| 1 |  |  |  |  |  |  |  | **3** |  | **3** |
| 2 |  |  |  |  |  |  |  |  | **5** | **5** |
| 3 |  | **1** |  |  |  |  |  | **5** |  | **6 (1 + 5)** |
| 4 |  |  |  |  |  |  |  | **4 + 1** |  | **5 (4 + 1)** |
| 5 |  | **1** | **2** |  |  |  |  |  |  | **3 (1 + 2)** |
| 6 |  |  | **2** |  |  |  |  |  |  | **2** |
| 7 |  |  | **1** |  |  |  | **5** |  |  | **6** |
| 8 |  |  | **1 + 2 + 2** |  | **1 + 2** |  | **3 + 1+ 1** |  |  | **13 (5 + 5 + 3)** |
| 9 -0 |  |  | **2** |  |  |  |  |  |  | **2** |
| 9 -1 |  |  |  |  |  | **6** |  |  |  | **6** |
| 9 -2 |  |  |  |  |  |  | **4** | **3+2+5** |  | **14 (3 + 2+ 9)** |
| 9 -3 | **3 + 5** | **1 + 1 + 5** | **1 + 2 + 13** | **1** |  |  | **1 + 3** |  |  | **36 (3 + 6 + 27)** |
| total | 8 | 9 | 31 | 1 | 3 | 6 | 18 | 23 | 5 | 104 |

## Figure S1. Conceptual workflow used for the clustering of 104 aerosol compounds.



## Figure S2. PCA loading plot\*.



\*Legend of descriptors (see Table S5)*: 2-D-Space constitutional descriptors:* 1) nAtom, 2) nBondsD2, 3) C3SP2, 4) C1SP3, 5) C2SP3, 6) C3SP3, 7) C4SP3, 8) nFRing, 9) nHeteroRing, 10) nRotBt; *2-D-Space electronic properties descriptors:* 11) ETA\_dEpsilon\_C, 12) nHBAcc\_Lipinski, 13) nHBDon\_Lipinski; *2-D-Space topological descriptors:* 14) ETA\_Eta\_B, 15) MPC2, 16) MPC7; *2-D-Space shape descriptors:* 17) ETA\_Shape\_X, 18) topoShape; *Physico-chemical descriptors:* 19) XLogP, 20) apol, 21) FMF, 22) MLFER\_S, 23) acd\_LogP\_Consensus, 24) HOMO (eV), 25) LUMO(eV); *Mechanistic descriptors (DNA alerts):* 26) AN2 >> Michael-type addition on alpha, beta-unsaturated carbonyl compounds >> Four- and Five-Membered Lactones, 27) AN2 >> Michael-type addition, quinoid structures >> Quinones, 28) AN2 >> Nucleophilic addition to alpha, beta-unsaturated carbonyl compounds >> alpha, beta-Unsaturated Aldehydes, 29) AN2 >> Schiff base formation >> alpha, beta-Unsaturated Aldehydes, 30) AN2 >> Schiff base formation >> Dicarbonyl compounds, 31) No alerts(DNA binding OASIS v.1.3), 32) Non-covalent interaction >> DNA intercalation >> Fused-Ring Nitroaromatics, 33) Non-covalent interaction >> DNA intercalation >> Quinones, 34) Radical >> Radical mechanism by ROS formation (indirect) or direct radical attack on DNA >> Organic Peroxy Compounds, 35) Radical >> Radical mechanism via ROS formation (indirect) >> Fused-Ring Nitroaromatics, 36) Radical >> Radical mechanism via ROS formation (indirect) >> Nitrophenols, Nitrophenyl Ethers and Nitrobenzoic Acids, 37) Radical >> Radical mechanism via ROS formation (indirect) >> Quinones, 38) SN1 >> Alkylation after metabolically formed carbenium ion species >> Polycyclic Aromatic Hydrocarbon Derivatives, 39) SN1 >> Nucleophilic attack after carbenium ion formation >> N-Nitroso Compounds, 40) SN1 >> Nucleophilic attack after carbenium ion formation >> Specific Acetate Esters, 41) SN1 >> Nucleophilic attack after nitrenium and/or carbenium ion formation >> N-Nitroso Compounds, 42) SN1 >> Nucleophilic attack after reduction and nitrenium ion formation >> Fused-Ring Nitroaromatics, 43) SN1 >> Nucleophilic attack after reduction and nitrenium ion formation >> Nitrophenols, Nitrophenyl Ethers and Nitrobenzoic Acids, 44) SN2 >> Acylation >> Specific Acetate Esters, 45) SN2 >> Alkylation, direct acting epoxides and related >> Epoxides and Aziridines, 46) SN2 >> Alkylation, direct acting epoxides and related after P450-mediated metabolic activation >> Polycyclic Aromatic Hydrocarbon Derivatives, 47) SN2 >> Alkylation, ring opening SN2 reaction >> Four- and Five-Membered Lactones, 48) SN2 >> Nucleophilic substitution at sp3 Carbon atom >> Specific Acetate Esters, 49) No alerts (DNA alerts for AMES, MN and CA by OASIS v.1.3), 50) Schiff base formers >> Direct Acting Schiff Base Formers >> Mono aldehydes, 51) SN1 >> Iminium Ion Formation >> Aliphatic tertiary amines, 52) Schiff base formers >> Direct Acting Schiff Base Formers >> Alpha-beta-dicarbonyl, 53) SN1 >> Nitrenium Ion formation >> Aromatic nitro, 54) Michael addition >> P450 Mediated Activation to Quinones and Quinone-type Chemicals >> Alkyl phenols, 55) Michael addition >> Polarised Alkenes-Michael addition >> Alpha, beta- unsaturated ketones, 56) Michael addition >> P450 Mediated Activation to Quinones and Quinone-type Chemicals >> Hydroquinones, 57) SN1 >> Carbenium Ion Formation >> Polycyclic (PAHs) and heterocyclic (HACs) aromatic hydrocarbons-SN1, 58) SN1 >> Carbenium Ion Formation >> N-Nitroso (alkylation), 59) SN2 >> Direct Acting Epoxides and related >> Epoxides, 60) Michael addition >> Quinones and Quinone-type Chemicals >> Quinones, 61) SN2 >> Nitrosation-SN2 >> Nitroso-SN2, 62) No alerts (DNA binding OECD); *Mechanistic descriptors (in vivo mutagenicity):* 63) 9,10-dihydrophenanthrenes, 64) Alkyl and aryl N-nitroso groups, 65) Alkyl hydroperoxides, 66) Epoxides and aziridines, 67) Nitro-aromatic, 68) Polycyclic Aromatic Hydrocarbons, 69) Quinones, 70) Simple aldehyde, 71) alpha,beta-unsaturated carbonyls, 72) No alerts(in vitro ISS), 73) H-acceptor-path3-H-acceptor, 74) Oxolane, 75) No alerts(in vivo ISS).

1. *K. Hansen et al. (2009) J. Chem. Inf. Model. 49 (9), pp 2077- 2081.* [↑](#footnote-ref-1)
2. *D. Kirkland, M. Aardemab, L. Henderson and L. Mueller (2005).* [↑](#footnote-ref-2)
3. *http://monographs.iarc.fr/index.php.* [↑](#footnote-ref-3)