Annex I –(Q)SAR model reporting format

(QMRF) v.2.1

QMRF v.2.1 is a minor update of the QMRF template, as it only concerns the description of the QMRF fields. The only exception is Section 10, which has been entirely removed. This section referred to the JRC QSAR Model Database, which is not updated anymore.

The update is based on the version 2.0[1].

	Element	Explanation
1.	**QSAR identifier**	
1.1.	QSAR identifier (title)	Volume of distribution at steady state (INERIS/Université Paris Cité/Inserm) (version 1.0.1)
1.2	Other related models	[1–4]
1.3.	Software coding the model	python 3.9.7
2.	**General information**	

[1] Triebe, J., Worth, A., Janusch Roi, A. and Coe, A., JRC QSAR Model Database: EURL ECVAM DataBase service on ALternative Methods to animal experimentation: To promote the development and uptake of alternative and advanced methods in toxicology and biomedical sciences: User Support & Tutorial, EUR 28713 EN, Publications Office of the European Union, Luxembourg, 2017, ISBN 978-92-79-71406-1, doi:10.2760/905519, JRC107491.

2.0	Abstract	We developed a machine learning QSAR model to predict the volume of distribution at steady state (VD_{ss}).VDss is an important Toxicokinetics (TK) property whose prediction is important for the characterization of TK propensities of potential drug candidates and for the assessment of chemical risk It is essential for safety assessment and for a comprehensive description of chemical toxicity.
2.1.	Date of QMRF	11 February 2025
2.2.	QMRF author(s) and contact details	Guillaume Ollitrault, Inserm U1133, CNRS UMR 8251, Université de Paris Cité, Paris, France. guillaume.ollitrault@inserm.fr Olivier Taboureau, Inserm U1133, CNRS UMR 8251, Université de Paris Cité, Paris, France. olivier.taboureau@univ-paris-diderot.fr Enrico Mombelli, Institut National de l'Environnement Industriel et des Risques (INERIS), Verneuil en Halatte, France. Enrico.MOMBELLI@ineris.fr
2.3.	Date of QMRF update(s)	NA
2.4.	QMRF update(s)	NA
2.5.	Model developer(s) and contact details	[1] Guillaume Ollitrault, Inserm U1133, CNRS UMR 8251, Université de Paris Cité, Paris, France. guillaume.ollitrault@inserm.fr [2] Olivier Taboureau, Inserm U1133, CNRS UMR 8251, Université de Paris Cité, Paris, France. olivier.taboureau@univ-paris-diderot.fr [3] Enrico Mombelli, Institut National de l'Environnement Industriel et des Risques (INERIS), Verneuil en Halatte, France. Enrico.MOMBELLI@ineris.fr
2.6.	Date of model development and/or publication	11 February 2025
2.7.	Reference(s) to main scientific papers and/or software package	Ollitrault G., Marzo M., Roncaglioni A., Taboureau O., Mombelli E,. (2025) "QSAR models for Oral Bioavailability and volume of distribution and their application to the mapping of the TK space of Endocrine Disruptors"
2.8.	Availability of information about the model	The model is non-proprietary: full description of the model algorithm is available (python scripts).Training and test sets are available as supplementary material of original research article together with molecular descriptor values for each modelled chemical
2.9.	Availability of another QMRF for exactly the same model	NA
3	**Defining the endpoint - OECD Principle 1: "A DEFINED ENDPOINT"**	**PRINCIPLE 1: "A DEFINED ENDPOINT". ENDPOINT refers to any physicochemical, biological, or environmental property/activity/effect that can be measured and therefore modelled. The intent of PRINCIPLE 1 (a (Q)SAR should be associated with a defined endpoint) is to ensure clarity in the endpoint being predicted by a given model, since a given endpoint could be determined by different experimental protocols and under different experimental conditions. It is therefore important to identify the experimental system and test conditions that is being modelled by the Q)SAR.**
3.1.	Species	Homo Sapiens
3.2.	Endpoint	5. Toxicokinetics. Human Volume of Distribution at steady state

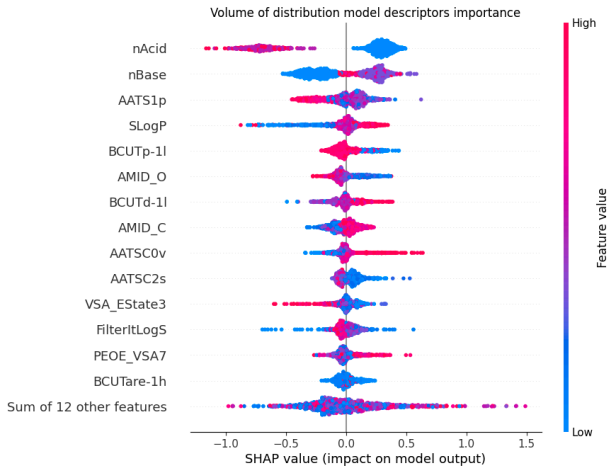
3.3	Comment on endpoint	The volume of distribution at steady state(VDss) measures the ability of a chemical to remain in plasma or to redistribute to other tissue compartments. VDss is computed by considering the amount of a chemical in the body divided by the plasma concentration of the same chemical. It is determined during the steady-state dosing of the xenobiotics of interest [5,6]
3.4.	Endpoint units	Regression : L/Kg
3.5.	Dependent variable	VDss in L/Kg
3.6.	Experimental protocol	VDss calculation is explained by Mansoor et al. [7]. VDss were retrieved from multiple sources including CHEMBL [8]the article by Lombardo et.al [1], Liu et al. [9]. In total, 1591 chemicals with associated VDss values were retrieved and curated.
3.7.	Endpoint data quality and variability	NA
4	**Defining the algorithm - OECD Principle 2 : "AN UNAMBIGUOUS ALGORITHM"**	**PRINCIPLE 2: "AN UNAMBIGUOUS ALGORITHM". The (Q)SAR estimate of an endpoint is the result of applying an ALGORITHM to a set of structural parameters which describe the chemical structure. The intent of PRINCIPLE 2 (a (Q)SAR should be associated with an unambiguous algorithm) is to ensure transparency in the model algorithm that generates predictions of an endpoint from information on chemical structure and/or physicochemical properties. In this context, algorithm refers to any mathematical equation, decision rule or output approach.**
4.1.	Type of model	Statistical QSAR model using a Random Forest (RF) algorithm as the quantitative classification.
4.2.	Explicit algorithm	Random forest [10] is an ensemble learning method that combines the output of multiple decision trees to make a prediction. Model was optimized on the training set with grid search optimizing the "min_samples_leaf", "max_depth" and the "min_samples_split". The best model resulted in a "min_samples_leaf" of 2, a "max_depth" set to none and a "min_samples_split" of 2.
4.3.	Descriptors in the model	26 mordred (v1.1.1) [11] molecular descriptors were retained covering physicochemical properties of the molecules. Molecular descriptors: AATSC0s; AATS0s; BCUTs-1h; AMID_O;AMID_C; nBase; EState_VSA10; FilterItLogS; AATSC0are; nAcid; AATSC0v; NaasC; BCUTd-1l; BCUTp-1l; SLogP; PEOE_VSA7; BCUTare-1h; GATS2are; C3SP2; AATSC1c; VSA_EState3; AATSC2s; AATS1p; ATSC6are; GATS2c; SaasC
4.4.	Descriptor selection	The VSURF [12] algorithm was applied to select and retain the most informative molecular descriptors. The R package VSURF allows to identify most informative molecular descriptors using random forest importance scores based on permutation and using a stepwise forward strategy that selects the variables of the most accurate models. VSURF identifies two sets of molecular descriptors: the interpretation and the prediction level. We selected the interpretation set as it contains the most molecular descriptors.
4.5.	Algorithm and descriptor generation	We computed Mordred molecular descriptors [11] as a function of normalized SMILES codes (see 6.6)

4.6.	Software name and version for descriptor generation	Mordred molecular descriptors v1.1.1 [11]
4.7.	Chemicals/Descriptors ratio	Topliss ratio of 45:1
5	**Defining the applicability domain - OECD Principle 3: "A DEFINED DOMAIN OF APPLICABILITY"**	**PRINCIPLE 3: "A DEFINED DOMAIN OF APPLICABILITY". APPLICABILITY DOMAIN refers to the response and chemical structure space in which the model makes predictions with a given reliability. Ideally the applicability domain should express the structural, physicochemical and response space of the model. The CHEMICAL STRUCTURE (x variable) space can be expressed by information on physicochemical properties and/or structural fragments. The RESPONSE (y variable) can be any physicochemical, biological or environmental effect that is being predicted. According to PRINCIPLE 3 a (Q)SAR should be associated with a defined domain of applicability. Section 5 can be repeated (e.g., 5.a, 5.b, 5.c, etc) as many times as necessary if more than one method has been used to assess the applicability domain.**
5.1.	Description of the applicability domain of the model	Structural Alert based approach
5.2.	Method used to assess the applicability domain	The likelihood ratio (LR) for each structural alert (SA) developed with SARpy [13,14] associated with each predicted chemical was considered to gauge its precision in predicting a chemical in a certain category of the SARpy model. SARpy applicability domain model was trained on the training set categorised in 3 class low, medium and high values of VDss considering 0.6 and 5 L/Kg thresholds. A chemical was deemed within the applicability domain if the LR of the structural alert responsible for the predicted compound exceeded 2.40. Threshold of 2.40 allowed to consider 63% of chemicals inside the AD of the external validation set.
5.3.	Software name and version for applicability domain assessment	Structural Alert based approach : SARpy
5.4.	Limits of applicability	Structural Alert based approach : A chemical was deemed within the applicability domain if the LR of the structural alert responsible for the predicted compound exceeded 2.40.
6	**Defining goodness-of-fit and robustness (internal validation) – OECD Principle 4: "APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTENESS AND PREDICTIVITY"**	**PRINCIPLE 4: "APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTENESS AND PREDICTIVITY". PRINCIPLE 4 expresses the need to perform validation to establish the performance of the model. GOODNESS-OF-FIT and ROBUSTNESS refer to the internal model performance.**
6.1.	Availability of the training set	It is available as supporting information of the cited article (see 2.7)
6.2.	Available information for the training set	Available information :Chemical names (common names and/or IUPAC names); SMILES
6.3.	Data for each descriptor variable for the training set	It is available as supporting information of the cited article (see 2.7)
6.4.	Data for the dependent variable for the training set	It is available as supporting information of the cited article (see 2.7)

<table>
<tr><td>6.5.</td><td>Other information about the training set</td><td>Molecules were assigned to the training set by sorting the chemicals based on their VDss values. Every fourth chemical was excluded from the training set and included in the validation set</td></tr>
<tr><td>6.6.</td><td>Pre-processing of data before modelling</td><td>All the chemicals were mapped to their pubchem Compound ID (CID) in order to have standardized chemical structures according to the pubchem protocol [15] (i.e normalization of the representation, implicit hydrogens atom valence, tautomeric form representation, etc …). The pubchem CID was retrieved according to the available SMILES, CAS RN, name, InChI available from the source database. In the case of chemicals with ions the largest fragment was considered. This standardization allowed us to identify duplicate chemicals for which we computed the mean VDss values. Only processed data is provided as supporting information of the cited article (see2.7).</td></tr>
<tr><td>6.7.</td><td>Statistics for goodness-of-fit</td><td>- Regression :
<table><tr><td>GMFE</td><td>1.37</td></tr></table>- Classification (1L/Kg Threshold) :
The regression model was evaluated for it’s ability to predict dichotomized classes of low or high VDss values considering a 1L/Kg thresholds.
<table><tr><td>Sensitivity</td><td>0.94</td></tr><tr><td>Specificity</td><td>0.90</td></tr><tr><td>Balanced accuracy</td><td>0.92</td></tr></table>- Multiclass classification (0.6L/Kg-5L/Kg Threshold) :
The regression model was evaluated for it’s ability to predict multi class of low, medium or high VDss values considering a 0.6L/Kg and 5L/Kg thresholds.
<table><tr><td>Sensitivity (<0.6L/Kg)</td><td>0.87</td></tr><tr><td>Specificity (<0.6L/Kg)</td><td>0.96</td></tr><tr><td>Balanced accuracy (<0.6L/Kg)</td><td>0.69</td></tr><tr><td>Sensitivity [0.6L/Kg-5L/Kg]</td><td>0.98</td></tr><tr><td>Specificity [0.6L/Kg-5L/Kg]</td><td>0.82</td></tr><tr><td>Balanced accuracy [0.6L/Kg-5L/Kg]</td><td>1</td></tr><tr><td>Sensitivity (>5L/Kg)</td><td>0.92</td></tr><tr><td>Specificity (>5L/Kg)</td><td>0.89</td></tr><tr><td>Balanced accuracy (>5L/Kg)</td><td>0.84</td></tr><tr><td>Macro Sensitivity</td><td>0.84</td></tr><tr><td>Macro Specificity</td><td>0.93</td></tr><tr><td>Macro Balanced accuracy</td><td>0.89</td></tr><tr><td>Micro Sensitivity</td><td>0.88</td></tr><tr><td>Micro Specificity</td><td>0.94</td></tr><tr><td>Micro Balanced accuracy</td><td>0.91</td></tr></table></td></tr>
<tr><td>6.8.</td><td>Robustness - Statistics obtained by leave-one-out cross-validation</td><td>NA</td></tr>
<tr><td>6.9.</td><td>Robustness - Statistics obtained by leave-many-out cross-validation</td><td>5-fold cross validation :
- Regression :
<table><tr><td>GMFE</td><td>2.19 ±0.08</td></tr></table>- Classification (1L/KgThreshold) :
The regression model was evaluated for its ability to predict dichotomized classes of low or high VDss values considering a 1L/Kg</td></tr>
</table>

<table>
<tr><td></td><td></td><td>thresholds.<table><tr><td>Sensitivity</td><td>0.79 ± 0.03</td></tr><tr><td>Specificity</td><td>0.75 ± 0.03</td></tr><tr><td>Balanced accuracy</td><td>0.77 ± 0.02</td></tr></table>- Multiclass classification (0.6L/Kg-5L/Kg Threshold) :
The regression model was evaluated for it's ability to predict multi class of low, medium or high VDss values considering a 0.6L/Kg and 5L/Kg thresholds.<table><tr><td>Sensitivity (<0.6L/Kg)</td><td>0.66 ± 0.04</td></tr><tr><td>Specificity (<0.6L/Kg)</td><td>0.90 ± 0.02</td></tr><tr><td>Balanced accuracy (<0.6L/Kg)</td><td>0.78 ± 0.02</td></tr><tr><td>Sensitivity [0.6L/Kg-5L/Kg]</td><td>0.83 ± 0.03</td></tr><tr><td>Specificity [0.6L/Kg-5L/Kg]</td><td>0.57 ± 0.04</td></tr><tr><td>Balanced accuracy [0.6L/Kg-5L/Kg]</td><td>0.70 ± 0.02</td></tr><tr><td>Sensitivity (>5L/Kg)</td><td>0.32 ± 0.06</td></tr><tr><td>Specificity (>5L/Kg)</td><td>0.97 ± 0.01</td></tr><tr><td>Balanced accuracy (>5L/Kg)</td><td>0.64 ± 0.03</td></tr></table></td></tr>
<tr><td>6.10.</td><td>Robustness - Statistics obtained by Y-scrambling</td><td>NA</td></tr>
<tr><td>6.11.</td><td>Robustness - Statistics obtained by bootstrap</td><td>NA</td></tr>
<tr><td>6.12.</td><td>Robustness - Statistics obtained by other methods</td><td>NA</td></tr>
<tr><td>7</td><td>Defining predictivity (external validation) – OECD Principle 4: "APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTENESS AND PREDICTIVITY"</td><td>PRINCIPLE 4: "APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTENESS AND PREDICTIVITY". PRINCIPLE 4 expresses the need to perform validation to establish the performance of the model. PREDICTIVITY refers to the external model validation. Section 7 can be repeated (e.g., 7.a, 7.b, 7.c, etc) as many times as necessary if more validation studies need to be reported in the QMRF.</td></tr>
<tr><td>7.1.</td><td>Availability of the external validation set</td><td>It is available as supporting information of the cited article (see 2.7)</td></tr>
<tr><td>7.2.</td><td>Available information for the external validation set</td><td>Available information : a) Chemical names (common names and/or IUPAC names); b) SMILES</td></tr>
<tr><td>7.3.</td><td>Data for each descriptor variable for the external validation set</td><td>NA</td></tr>
<tr><td>7.4.</td><td>Data for the dependent variable for the external validation set</td><td>It is available as supporting information of the cited article (see 2.7)</td></tr>
<tr><td>7.5.</td><td>Other information about the external validation set</td><td>External validation set with 390 compounds</td></tr>
<tr><td>7.6.</td><td>Experimental design of test set</td><td>Molecules in the external set were selected by sorting VDss values and we included every fourth chemical to this set, ensuring representative inclusion across the range of VDss values</td></tr>
<tr><td>7.7.</td><td>Predictivity - Statistics obtained by external validation</td><td>- Regression :<table><tr><td>GMFE</td><td>2.35</td></tr></table>- Classification (1L/Kg Threshold) :
The regression model was evaluated for its ability to predict dichotomized classes of low or high VDss values considering a 1L/Kg</td></tr>
</table>

<table>
<tr><td></td><td></td><td>threshold.<table><tr><td>Sensitivity</td><td>0.79</td></tr><tr><td>Specificity</td><td>0.71</td></tr><tr><td>Balanced accuracy</td><td>0.75</td></tr></table>- Multiclass classification (0.6L/Kg-5L/Kg Threshold) :
The regression model was evaluated for it's ability to predict multi class of low, medium or high VDss values considering a 0.6L/Kg and 5L/Kg threshold.<table><tr><td>Sensitivity (<0.6L/Kg)</td><td>0.62</td></tr><tr><td>Specificity (<0.6L/Kg)</td><td>0.82</td></tr><tr><td>Balanced accuracy (<0.6L/Kg)</td><td>0.23</td></tr><tr><td>Sensitivity [0.6L/Kg-60%]</td><td>0.91</td></tr><tr><td>Specificity [0.6L/Kg-60%]</td><td>0.51</td></tr><tr><td>Balanced accuracy [0.6L/Kg-5L/Kg]</td><td>0.97</td></tr><tr><td>Sensitivity (>5L/Kg)</td><td>0.76</td></tr><tr><td>Specificity (>5L/Kg)</td><td>0.67</td></tr><tr><td>Balanced accuracy (>5L/Kg)</td><td>0.60</td></tr><tr><td>Macro Sensitivity</td><td>0.56</td></tr><tr><td>Macro Specificity</td><td>0.80</td></tr><tr><td>Macro Balanced accuracy</td><td>0.68</td></tr><tr><td>Micro Sensitivity</td><td>0.65</td></tr><tr><td>Micro Specificity</td><td>0.83</td></tr><tr><td>Micro Balanced accuracy</td><td>0.74</td></tr></table></td></tr>
<tr><td>7.8.</td><td>Predictivity - Assessment of the external validation set</td><td>NA</td></tr>
<tr><td>7.9.</td><td>Comments on the external validation of the model</td><td>The external set was composed of molecules not used during the training and the hyperparametrisation of the model.</td></tr>
<tr><td>8</td><td>Providing a mechanistic interpretation - OECD Principle 5: "A MECHANISTIC INTERPRETATION, IF POSSIBLE"</td><td>PRINCIPLE 5: "A MECHANISTIC INTERPRETATION, IF POSSIBLE". According to PRINCIPLE 5, a (Q)SAR should be associated with a mechanistic interpretation, if possible.</td></tr>
</table>

8.1.	Mechanistic basis of the model	 **Figure**. Summary plot obtained by using the SHAP package [16]. The plot shows the importance of the 15 most important molecular molecular descriptors and their effect on the predictions for the random forest model. The plot enables the observation of the relationship between a molecular descriptor value and its impact on the prediction. Low numbers of acid groups increase the VDss low numbers of base groups decrease VDss. Another important molecular descriptor is the SLogP .
8.2.	A priori or a posteriori mechanistic interpretation	The Mechanical basis of the model was determined a posteriori (i.e. after modelling, by interpretation of the final model).
8.3.	Other information about the mechanistic interpretation	acidic groups, base groups and logarithm of n-octanol-water partition coefficient molecular descriptors were previously found having an impact on VDss in the literature [17,18].
9	**Miscellaneous information**	
9.1.	Comments	NA
9.2.	Bibliography	1. Lombardo, F.; Bentzien, J.; Berellini, G.; Muegge, I. In Silico Models of Human PK Parameters. Prediction of Volume of Distribution Using an Extensive Data Set and a Reduced Number of Parameters. *J. Pharm. Sci.* **2021**, *110*, 500–509, doi:10.1016/j.xphs.2020.08.023. 2. Gombar, V.K.; Hall, S.D. Quantitative Structure–Activity Relationship Models of Clinical Pharmacokinetics: Clearance and Volume of Distribution. *J. Chem. Inf. Model.* **2013**, *53*, 948–957, doi:10.1021/ci400001u. 3. Fagerholm, U.; Hellberg, S.; Alvarsson, J.; Arvidsson McShane, S.; Spjuth, O. *In Silico* Prediction of Volume of Distribution of Drugs in Man Using Conformal Prediction Performs on Par with Animal Data-Based Models. *Xenobiotica* **2021**, *51*, 1366–1371, doi:10.1080/00498254.2021.2011471. 4. Simeon, S.; Montanari, D.; Gleeson, M.P. Investigation of Factors Affecting the Performance of *in Silico* Volume Distribution QSAR Models for Human, Rat, Mouse, Dog & Monkey. *Mol. Inform.* **2019**, *38*, 1900059, doi:10.1002/minf.201900059. 5. Shanmugam, P.S.T.; Sampath, T.; Jagadeeswaran, I.; Bhalerao, V.P.; Thamizharasan, S.; V., K.; Saha, J. Toxicokinetics. In *Biocompatibility Protocols for Medical Devices and Materials*; Elsevier, 2023; pp. 175–186 ISBN 978-0-323-91952-4. 6. Smith, D.A.; Beaumont, K.; Maurer, T.S.; Di, L. Volume of Distribution in Drug Design: Miniperspective. *J. Med. Chem.* **2015**, *58*, 5691–5698, doi:10.1021/acs.jmedchem.5b00201. 7. Mansoor, A.; Mahabadi, N. Volume of Distribution. In *StatPearls*; StatPearls Publishing: Treasure Island (FL), 2025. 8. Gaulton, A.; Bellis, L.J.; Bento, A.P.; Chambers, J.; Davies, M.;

		Hersey, A.; Light, Y.; McGlinchey, S.; Michalovich, D.; Al-Lazikani, B.; et al. ChEMBL: A Large-Scale Bioactivity Database for Drug Discovery. *Nucleic Acids Res.* **2012**, *40*, D1100–D1107, doi:10.1093/nar/gkr777. 9. Liu, W.; Luo, C.; Wang, H.; Meng, F. A Benchmarking Dataset with 2440 Organic Molecules for Volume Distribution at Steady State. **2022**, doi:10.48550/ARXIV.2211.05661. 10. Breiman, L. Random Forests. *Mach. Learn.* **2001**, *45*, 5–32, doi:10.1023/A:1010933404324. 11. Moriwaki, H.; Tian, Y.-S.; Kawashita, N.; Takagi, T. Mordred: A Molecular Descriptor Calculator. *J. Cheminformatics* **2018**, *10*, 4, doi:10.1186/s13321-018-0258-y. 12. Genuer, R.; Poggi, J.-M.; Tuleau-Malot, C. VSURF: An R Package for Variable Selection Using Random Forests. *R J.* **2015**, *7*, 19, doi:10.32614/RJ-2015-018. 13. Ferrari, T.; Gini, G.; Golbamaki Bakhtyari, N.; Benfenati, E. Mining Toxicity Structural Alerts from SMILES: A New Way to Derive Structure Activity Relationships. In Proceedings of the 2011 IEEE Symposium on Computational Intelligence and Data Mining (CIDM); IEEE: Paris, France, April 2011; pp. 120–127. 14. Ferrari, T.; Cattaneo, D.; Gini, G.; Golbamaki Bakhtyari, N.; Manganaro, A.; Benfenati, E. Automatic Knowledge Extraction from Chemical Structures: The Case of Mutagenicity Prediction. *SAR QSAR Environ. Res.* **2013**, *24*, 365–383, doi:10.1080/1062936X.2013.773376. 15. Hähnke, V.D.; Kim, S.; Bolton, E.E. PubChem Chemical Structure Standardization. *J. Cheminformatics* **2018**, *10*, 36, doi:10.1186/s13321-018-0293-8. 16. Lundberg, S.M.; Lee, S.-I. A Unified Approach to Interpreting Model Predictions. In *Advances in Neural Information Processing Systems 30*; Guyon, I., Luxburg, U.V., Bengio, S., Wallach, H., Fergus, R., Vishwanathan, S., Garnett, R., Eds.; Curran Associates, Inc., 2017; pp. 4765–4774. 17. Skakkebæk, N.E.; Lindahl-Jacobsen, R.; Levine, H.; Andersson, A.-M.; Jørgensen, N.; Main, K.M.; Lidegaard, Ø.; Priskorn, L.; Holmboe, S.A.; Bräuner, E.V.; et al. Environmental Factors in Declining Human Fertility. *Nat. Rev. Endocrinol.* **2022**, *18*, 139–157, doi:10.1038/s41574-021-00598-8. 18. Watanabe, J.; Kozaki, A. Relationship between Partition Coefficients and Apparent Volumes of Distribution for Basic Drugs. II. *Chem. Pharm. Bull. (Tokyo)* **1978**, *26*, 3463–3470, doi:10.1248/cpb.26.3463.
9.3	Supporting information	NA