# 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]](#footnote-1).

|  |  |  |
| --- | --- | --- |
|  | **Element** | **Explanation** |
| **1.** | **QSAR identifier** |  |
| 1.1. | QSAR identifier (title) | QSPRpred QSAR model for thyroid hormone receptor beta binding. |
| 1.2 | Other related models |  |
| 1.3. | Software coding the model | Software coding the model: qsprpred  Version info [from git repo]: (main) v4.0.0.alpha1+2[d742e8ff]+dirty |
| **2.** | **General information** |  |
| 2.0 | Abstract | This model was developed to predict MIE activation in context of the thyroid mediated neurotoxicity AOP. |
| 2.1. | Date of QMRF | 2025-03-26 14:29:22 |
| 2.2. | QMRF author(s) and contact details | Linde Schoenmaker (l.schoenmaker@lacdr.leidenuniv.nl) |
| 2.3. | Date of QMRF update(s) |  |
| 2.4. | QMRF update(s) |  |
| 2.5. | Model developer(s) and contact details | Linde Schoenmaker (l.schoenmaker@lacdr.leidenuniv.nl) |
| 2.6. | Date of model development and/or publication | Creation date: 2025-03-26 14:13:53 |
| 2.7. | Reference(s) to main scientific papers and/or software package | References to main scientific papers and/or software package: homepage, https://github.com/CDDLeiden/QSPRpred; repository, https://github.com/CDDLeiden/QSPRpred; documentation, https://cddleiden.github.io/QSPRpred/docs/ |
| 2.8. | Availability of information about the model | Model is non-proprietary: training and test sets are available in model repository X |
| 2.9. | Availability of another QMRF for exactly the same model |  |
| **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 | Protein-binding |
| 3.3 | Comment on endpoint | Comment on endpoint: uniprot accessions P, 1, 0, 8, 2, 8 |
| 3.4. | Endpoint units | Endpoint units: IC50, EC50, KD, Ki, other |
| 3.5. | Dependent variable | For modelling purposes the bioactivity values were transformed to logarithmic units. The dependent variable is defined as: -Log(molar IC50, XC50, EC50, AC50, Ki, Kd or Potency). |
| 3.6. | Experimental protocol |  |
| 3.7. | Endpoint data quality and variability | Endpoint data quality and variability: bioactivity data was collected from Papyrus 05.7. Minimum data quality high |
| **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 | QSAR |
| 4.2. | Explicit algorithm | Explicit algorithm: RandomForestRegressor as implemented in scikit-learn 1.4.0 |
| 4.3. | Descriptors in the model | Descriptors in the model: MorganFP, 2048 features |
| 4.4. | Descriptor selection |  |
| 4.5. | Algorithm and descriptor generation | Descriptor generation MorganFP: idProp=QSPRID, radius=3, nBits=2048, kwargs={} |
| 4.6. | Software name and version for descriptor generation | Software name and version for descriptor generation: rdkit 2024.9.6 |
| 4.7. | Chemicals/Descriptors ratio | Chemicals/Descriptors ratio TRbeta: 0.13; 272 chemicals/2048 descriptors |
| **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 | k-Nearest Neighbors (KNN) is used for AD evaluation. The distance of the predicted compound to the nearest neighbors in the training set is compared to a threshold. The applicability domain threshold is based on the 95% percentile of the training set. Attached in the supporting information is a figure of the residuals plotted against the KNN distance. |
| 5.2. | Method used to assess the applicability domain | Method used to assess the applicability domain: KNNApplicabilityDomain |
| 5.3. | Software name and version for applicability domain assessment | Software name and version for applicability domain assessment: scikit-learn 1.4.0 |
| 5.4. | Limits of applicability | Limits of applicability: molecule is within AD when distance is < the distance of the 95% percentile compared to training data. |
| **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 |  |
| 6.2. | Available information for the training set |  |
| 6.3. | Data for each descriptor variable for the training set |  |
| 6.4. | Data for the dependent variable for the training set |  |
| 6.5. | Other information about the training set |  |
| 6.6. | Pre-processing of data before modelling |  |
| 6.7. | Statistics for goodness-of-fit |  |
| 6.8. | Robustness - Statistics obtained by leave-one-out cross-validation |  |
| 6.9. | Robustness - Statistics obtained by leave-many-out cross-validation | Robustness - Statistics obtained by leave-many-out cross-validation: r2\_score = [0.5703125221478548, 0.5006942114245928, 0.5073246320691513, 0.631654559973666, 0.15910591394186047] |
| 6.10. | Robustness - Statistics obtained by Y-scrambling |  |
| 6.11. | Robustness - Statistics obtained by bootstrap |  |
| 6.12. | Robustness - Statistics obtained by other methods |  |
| **7** | **Defining predictivity (external 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. 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.** |
| 7.1. | Availability of the external validation set |  |
| 7.2. | Available information for the external validation set |  |
| 7.3. | Data for each descriptor variable for the external validation set |  |
| 7.4. | Data for the dependent variable for the external validation set |  |
| 7.5. | Other information about the external validation set |  |
| 7.6. | Experimental design of test set |  |
| 7.7. | Predictivity - Statistics obtained by external validation | Robustness - Statistics obtained by test: r2\_score = [0.6204468506413406] |
| 7.8. | Predictivity - Assessment of the external validation set |  |
| 7.9. | Comments on the external validation of the model |  |
| **8** | **Providing a mechanistic interpretation - OECD Principle 5: “A MECHANISTIC INTERPRETATION, IF POSSIBLE”** | **PRINCIPLE 5: “A MECHANISTIC INTERPRETATION, IF POSSIBLE”. According to PRINCIPLE 5, a (Q)SAR should be associated with a mechanistic interpretation, if possible.** |
| 8.1. | Mechanistic basis of the model |  |
| 8.2. | A priori or a posteriori mechanistic interpretation |  |
| 8.3. | Other information about the mechanistic interpretation |  |
| **9** | **Miscellaneous information** |  |
| 9.1. | Comments |  |
| 9.2. | Bibliography |  |
| 9.3 | Supporting 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. [↑](#footnote-ref-1)