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ENVIRONMENT DIRECTORATE
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ANNEX I – (Q)SAR model reporting format (QMRF) v.2.1

**Series on Testing and Assessment
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The (Q)SAR Assessment Framework document is available under the cote ENV/CBC/MONO(2023)32

An editable format is available at

<https://www.oecd.org/chemicalsafety/risk-assessment/qsar-assessment-framework-annex-1-qsar-model-reporting-format.docx>

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SERIES ON TESTING AND ASSESSMENT
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ANNEX I – (Q)SAR model reporting format (QMRF) v.2.1

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among **FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD**

Environment Directorate
ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT
Paris 2023

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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 2.0¹.

	Element	Explanation
1.	QSAR identifier	
1.1.	QSAR identifier (title)	Provide the title of the model. The title should include keywords such as: endpoint modelled (as detailed as possible and consistent with section 3 of the QMRF, recommended), name of the model, name of the modeller, and name of the software and version coding the model. Examples: “ <i>EPI Suite™</i> BIOWIN v4.10 for Biodegradation”; “TOPKAT Rabbit Skin Irritation (Draize test) for Acyclic compounds (Acids, Amines, Esters) Severe vs Non/Mild/Moderate skin irritation”.
1.2	Other related models	If applicable, identify any model that is related to the model described in the present QMRF. Example: TOPKAT Rabbit Skin Irritation (Draize test) for Acyclics compounds (Acids, Amines, Esters) NEG/MLD v MOD/SEV Model Nonirritant vs. Mild/Moderate skin irritation” is related to the model mentioned in 1.1: “TOPKAT Skin Irritation Acyclics compounds (Acids, Amines, Esters) Severe vs. Non/Mild/Moderate skin irritation MOD v SEV Model.”
1.3.	Software coding the model	Specify the name and the version of the software that implements the model. Examples: “BIOWIN v. 4.2 (EPI Suite)”; “TOPKAT v. 6.2”. If the model is implemented as a web service, please report link to the service. If no software implements the model, please state this.
2.	General information	
2.0	Abstract	A free text description of the context and background of the (Q)SAR model. In addition, a more comprehensive explanation should be added if there is no scientific article about the model or if the presented model is based on several scientific articles. If the model is adapted from a

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.

		scientific article, or from data obtained from open (or closed) sources, it must be clearly stated, and the changes made during the adoption of the model must be described.
2.1.	Date of QMRF	Report the date of QMRF drafting (day/month/year). Example: "5 November 2023".
2.2.	QMRF author(s) and contact details	QMRF author(s) and contact details: Indicate the name and the contact details of the author(s) of the QMRF (first version of the QMRF).
2.3.	Date of QMRF update(s)	Date of QMRF update(s): Indicate the date (day/month/year) of any update of the QMRF. The QMRF can be updated for a number of reasons such as additions of new information (e.g. addition of new validation studies in section 7) and corrections of information. However, please note that if the (Q)SAR itself is being updated (i.e. changes in training set or modelling) this should be regarded as a new model which should have a new QMRF, rather than an update of the old QMRF.
2.4.	QMRF update(s)	QMRF update(s): Indicate the name and the contact details of the author(s) of the QMRF updates (see field 2.3) and list which sections and fields have been modified and why.
2.5.	Model developer(s) and contact details	Model developer(s) and contact details: Indicate the name of model developer(s)/author(s), and the corresponding contact details; possibly report the contact details of the corresponding author.
2.6.	Date of model development and/or publication	Date of model development and/or publication: Report the year of release/publication of the model described in this QMRF.
2.7.	Reference(s) to main scientific papers and/or software package	Reference(s) to main scientific papers and/or software package: List the main bibliographic references (if any) to original paper(s) explaining the model development and/or software implementation. Any other reference such as references to original experimental data and related models can be reported in field 9.2 "Bibliography". Please note, that it should be clearly indicated if the scientific paper(s) refer to an earlier model version / model than the one addressed in the QMRF.
2.8.	Availability of information about the model	Availability of information about the model: Indicate whether the model is proprietary or non-proprietary and specify (if possible) what kind of information about the model cannot be disclosed or are not available (e.g., training and external validation sets, source code, and algorithm). Example: "The model is non-proprietary: full description of the model algorithm is available, training and test sets are available as supplementary material of original research article"; "The model is non-proprietary: training and test sets are available in model repository X"; "The model is non-proprietary: but the training and test sets are not available"; "The model is proprietary and: the algorithm and the data sets are confidential"; "The model is proprietary: the algorithm and data sets and model development are confidential, however the model is implemented in a public web service";
2.9.	Availability of another QMRF for exactly the same model	Availability of another QMRF for exactly the same model: Indicate if you are aware or suspect that another QMRF is available for the current model you are describing. If possible, identify this other QMRF.

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	Species: if applicable, indicate the species for the endpoint being modelled. Taxon, species, strain, clone, type of organism, cell type, or other (e.g., <i>in chemico</i>) Example: Fathead minnow (<i>Pimephales promelas</i>)
3.2.	Endpoint	Endpoint: describe the endpoint that is modelled. The experimental protocol(s) and test conditions applied for the training set data together with the subsequent data curation for (Q)SAR modelling determine the endpoint predicted by the model.
3.3	Comment on endpoint	Comment on the endpoint: Include in this field any other information to define the endpoint being modelled. Specify the endpoint further if relevant, e.g. according to test organism such as species, strain, sex, age or life stage; according to test duration and protocol; according to the detailed nature of endpoint etc.
3.4.	Endpoint units	Endpoint units: Specify the units of the endpoint measured. For categorical endpoints, provide details on the scale and eventual conversions.
3.5.	Dependent variable	Dependent variable: Specify the relationship between the dependent variable being modelled and the endpoint measured since the two quantities may be different. Example: For modelling purposes all rate constants (i.e. Nitrate radical degradation rate constant (kNO ₃)) were transformed to logarithmic units and multiplied by -1 to obtain positive values. The dependent variable is: -log(kNO ₃).
3.6.	Experimental protocol	Experimental protocol: Make any useful reference to a specific experimental protocol(s) (for example OECD Test Guideline number) followed in the collection and evaluation of the experimental data sets.
3.7.	Endpoint data quality and variability	Endpoint data quality and variability: provide available information about the experimental test data quality selection and evaluation and include a description of the data quality used to develop the model. This includes provision of information about in terms of the known variability of the test data, i.e. repeatability (variability over time) and reproducibility (variability between laboratories) and sources of error (confounding factors which may influence testing results) etc.. Please also as far as possible provide information about test chemical purity. Ideally, (Q)SARs should be based on experimental tests performed with test chemical of high purity to assure good correlation between structures and effect. Test chemical purity should preferably be provided for the individual

		<p>substances used in the training and validation sets.</p> <p>The data curation procedure and its effect on data quality should also be described here.</p>
4	Defining the algorithm - OECD Principle 2 : "AN UNAMBIGUOUS ALGORITHM"	<p>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.</p>
4.1.	Type of model	Type of model: Describe the type of model, e.g., equation based, fragment/alert based (expert rule-based and/or statistical based), etc..
4.2.	Explicit algorithm	<p>Explicit algorithm: Report the algorithm (only the algorithm) for generating predictions from the descriptors and/or structural fragments/alerts; more text information about the algorithm can be reported in the following fields of this section or as supporting information (see field 9.3). If the algorithm is too long and complicated, include in this field a reference to a scientific paper or another document where the algorithm and/or general modelling approach is described in detail. If possible, the algorithm should be made available in a machine-readable manner (e.g., PMML or some other model describing format). This material can be attached as supporting information or made available in an open access repository. This material can be attached as supporting information.</p> <p>If the algorithm cannot be disclosed or fully disclosed due to confidentiality, it should be explicitly stated.</p>
4.3.	Descriptors in the model	Descriptors in the model: Identify the number and the name or identifier of the descriptors included in the model. In this context, descriptors refer to e.g. physicochemical parameters, structural fragments etc.
4.4.	Descriptor selection	Descriptor selection: Indicate the number and the type (name) of descriptors /decision rules initially screened, and explain the method used to select the descriptors and develop the model from them.
4.5.	Algorithm and descriptor generation	Algorithm and descriptor generation: Explain the approach used to derive the algorithm and the method (approach) used to generate each descriptor.
4.6.	Software name and version for descriptor generation	Software name and version for descriptor and algorithm generation: Specify the name and the version of the software used to generate the descriptors and the algorithm. If relevant, report the specific settings chosen in the software to generate a descriptor or the algorithm.

4.7.	Chemicals/Descriptors ratio	Chemicals/ Descriptors ratio: Report the following ratio: number of chemicals (chemicals from the training set) to number of descriptors, if applicable (if not, explain why). For some type of models, it may also be important to report the number of other parameters in the model (e.g., number of hidden neurons in artificial neural network models).
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	Description of the applicability domain of the model: Define / describe the response and chemical structure and/or descriptor space in which the model makes predictions with a given reliability determined in the statistical validation. Describe the defined applicability domain in terms of the following, as relevant: a) fixed or probabilistic boundaries; b) structural features, a descriptor and/or a response space; c) in the case of (Q)SARs which applies substructures as descriptors, describe possible defined limits on applicability (inclusion and/or exclusion rules regarding the chemical classes to which the model is applicable); d) in the case of (Q)SARs applying substructures as descriptors, describe possible rules on the modularity effects of the substructure's molecular environment; e) possible defined inclusion and/or exclusion rules for the descriptor variable ranges for which the (Q)SAR is applicable; f) possible defined inclusion and/or exclusion rules that define the response variable ranges for which the QSAR is applicable; g) possible defined (graphical) expression of how the descriptor values of the chemicals in the training set are distributed in relation to the endpoint values predicted by the model.
5.2.	Method used to assess the applicability domain	Method used to assess the applicability domain: Describe the method used to assess the applicability domain of the model.
5.3.	Software name and version for applicability domain assessment	Software name and version for applicability domain assessment: Specify the name and the version of the software used to apply the applicability domain method, where applicable. If relevant, report the specific settings chosen in the software to apply the method.

5.4.	Limits of applicability	Limits of applicability: Describe for example the inclusion and/or exclusion rules (fixed or probabilistic boundaries, structural features, descriptor space, response space) that define the applicability domain.
6	Defining goodness-of-fit and robustness (internal validation) – OECD Principle 4: “APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTNESS AND PREDICTIVITY”	PRINCIPLE 4: “APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTNESS 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	Availability of the training set: Indicate whether the training set is somehow available (e.g., published in a paper, embedded in the software implementing the model, stored in a database) and appended to the current QMRF as supporting information (field 9.3). If it is not available, explain why. Example: “It is available and attached” “It is available but not attached”; “It is not available because the data set is proprietary”; “The data set could not be retrieved”.
6.2.	Available information for the training set	Available information for the training set: Indicate whether the following information for the training set is reported as supporting information (see field 9.3): a) Chemical names (common names and/or IUPAC names); b) CAS numbers; c) SMILES; d) InChI codes; e) MOL files; f) Structural formula; g) If the dataset contains nanomaterials; h) test chemical purity for individual substances; i) Any other structural information.
6.3.	Data for each descriptor variable for the training set	Data for each descriptor variable for the training set: Indicate whether the descriptor values of the training set are available and are attached as supporting information (see field 9.3).
6.4.	Data for the dependent variable for the training set	Data for the dependent variable (response) for the training set: Indicate whether dependent variable values of the training set are available and attached as supporting information (see field 9.3).
6.5.	Other information about the training set	Regardless of whether the training set is made available, other information about the training set: Indicate any other relevant information about the training set (e.g. number and type of compounds in the training set (e.g. for models predicting positive and negative results the number of positives and the number of negatives in the training set)). Also indicate the rationale on the selection of the different compounds of the training set here.
6.6.	Pre-processing of data before modelling	Pre-processing of data before modelling: Indicate whether raw data have been processed before modelling (e.g. averaging of replicate values); if yes, report whether both raw data and processed data are given.
6.7.	Statistics for goodness-of-fit	Statistics for goodness-of-fit: Report here goodness-of-fit statistics: in the case of models for continuous endpoints, report at least r^2 , r^2 adjusted, RMSE; in the case of models for categorical endpoints, report at least sensitivity, specificity, true positives (TP), true negatives (TN), false negatives (FN), false positives (FP)
6.8.	Robustness - Statistics obtained by leave-one-out cross-validation	Robustness – Statistics obtained by leave-one-out cross-validation: Report here the corresponding statistics.

6.9.	Robustness - Statistics obtained by leave-many-out cross-validation	Robustness – Statistics obtained by leave-many-out cross-validation: Report here the corresponding statistics, the strategy for splitting the data set (e.g. random, stratified), the percentage of left out compounds and the number of cross-validations.
6.10.	Robustness - Statistics obtained by Y-scrambling	Robustness – Statistics obtained by Y-scrambling: Report here the corresponding statistics and the number of iterations.
6.11.	Robustness - Statistics obtained by bootstrap	Robustness – Statistics obtained by bootstrap: Report here the corresponding statistics and the number of iterations.
6.12.	Robustness - Statistics obtained by other methods	Robustness – Statistics obtained by other methods: Report here the corresponding statistics.
7	Defining predictivity (external validation) – OECD Principle 4: “APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTNESS AND PREDICTIVITY”	PRINCIPLE 4: “APPROPRIATE MEASURES OF GOODNESS-OF-FIT, ROBUSTNESS 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	Availability of the external validation set: Indicate whether an external validation set is available and appended to the current QMRF as supporting information (field 9.3). If it is not available, explain why.
7.2.	Available information for the external validation set	Available information for the external validation set: Indicate whether the following information for the external validation set is reported as supporting information (see field 9.3): a) Chemical names (common names and/or IUPAC names); b) CAS numbers; c) SMILES; d) InChI codes; e) MOL files; f) Structural formula; g) If the dataset contains nanomaterials; h) test chemical purity for individual substances; i) Any other structural information.
7.3.	Data for each descriptor variable for the external validation set	Data for each descriptor variable for the external validation set: Indicate whether descriptor values of the external validation set are somehow available and attached as supporting information (see field 9.3).
7.4.	Data for the dependent variable for the external validation set	Data for the dependent variable for the external validation set: Indicate whether dependent variable values of the external validation set are somehow available and attached as supporting information (see field 9.3).
7.5.	Other information about the external validation set	Other information about the external validation set: Indicate any other relevant information about the validation set. Example: “External validation set with 56 compounds appended”.
7.6.	Experimental design of test set	Experimental design of test set: Indicate any experimental design for getting the validation set (e.g. by randomly setting aside chemicals before modelling, by literature search after modelling, by prospective experimental testing after modelling, etc.).
7.7.	Predictivity - Statistics obtained by external validation	Predictivity – Statistics obtained by external validation: Report here the corresponding statistics. In the case of classification models, include false positive and negative rates.

7.8.	Predictivity - Assessment of the external validation set	Predictivity – Assessment of the external validation set: Discuss whether the external validation set is sufficiently large and representative of the applicability domain. Describe for example the descriptor and response range or space for the validation test set as compared with that for the training set. Here the descriptor values of the chemicals predicted by the model (training set) should be compared with the descriptor value range of the test set. In addition, the distribution of the response values of the chemicals in the training set should be compared to the distribution of the response values of the test set. Predictivity of certain (Q)SARs can be measured by a cross-validation procedure qualifying it to be a “n-fold external validation procedure” or “external cross-validation”
7.9.	Comments on the external validation of the model	Comments on the external validation of the model: Add any other useful comments about the external validation procedure.
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	Mechanistic basis of the model: Provide information on the mechanistic basis of the model (if possible). In the case of (Q)SARs using structural features as descriptors, you may want to describe (if possible) the molecular features that underlie the properties of the molecules containing the substructure (e.g. a description of how sub-structural features could act as nucleophiles or electrophiles, or form part or all of a receptor-binding region). In the case of (Q)SARs using numeric descriptors, you may give (if possible) a physicochemical interpretation of the descriptors used (consistent with a known mechanism of biological action). If it is not possible to provide a mechanistic interpretation, try to explain why.
8.2.	A priori or a posteriori mechanistic interpretation	A priori or a posteriori mechanistic interpretation: Indicate whether the mechanistic basis of the model was determined a priori (i.e. before modelling, by ensuring that the initial set of training structures and/or descriptors were selected to fit pre-defined known mechanism of action) or a posteriori (i.e. after modelling, by interpretation of the final set of training structures and or descriptors).
8.3.	Other information about the mechanistic interpretation	Other information about the mechanistic interpretation: Report any other useful information about the (purported) mechanistic interpretation described in the previous fields (8.1 and 8.2) such as any reference supporting the mechanistic basis.
9	Miscellaneous information	
9.1.	Comments	Comments: Add here other relevant and useful comments (e.g. other related models, known applications of the model) that may facilitate regulatory considerations on the model described. Include if relevant experience obtained by use of model prediction for various types of regulatory decisions (incl. references as appropriate).
9.2.	Bibliography	Bibliography: Report useful references other than those directly associated with the model development (references describing the model development are reported in field 2.7).

9.3	Supporting information	Supporting information: Indicate whether supporting information is attached (e.g. external documents) to this QMRF and specify its content and possibly its utility. This should cover structures in the training, set, and validation sets, response variable value), descriptor values, whether the training and test sets are submitted in defined file formats (txt, csv, SDF, etc.), model (e.g., pmm), predictions for training and validation sets and other documents, as relevant.
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