QSAR Prediction Reporting Format (QPRF)

The adequacy of a prediction depends on the following conditions: a) **the (Q)SAR model is scientifically valid**: the scientific validity is established according to the OECD principles for (Q)SAR validation; b) **the (Q)SAR model is applicable to the query chemical**: a (Q)SAR is applicable if the query chemical falls within the defined applicability domain of the model; c) **the (Q)SAR result is reliable**: a valid (Q)SAR that is applied to a chemical falling within its applicability domain provides a reliable result; d) **the (Q)SAR model is relevant for the regulatory purpose**: the predicted endpoint can be used directly or following an extrapolation, possibly in combination with other information, for a particular regulatory purpose.

A (Q)SAR prediction (model result) may be considered adequate if it is reliable and relevant, and depending on the totality of information available in a weight-of-evidence assessment (see Section 4 of the QPRF).

1. Substance

1.1 CAS number:

50-00-0

1.2 EC number:

200-001-8

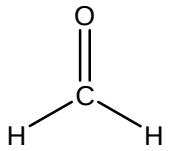
1.3 Chemical name:

Formaldehyde, methyl aldehyde

1.4 Structural formula:

CH_2O

1.5 Structure codes:



a. **SMILES**:

C=O , not used for prediction

b. **InChI:**

1/CH2O/c1-2/h1H2 , not used for prediction

c. **Other structural representation**:

Mol file used for prediction

d. **Stereochemical features:**

n/a

2. General information

Date of QPRF:

02.06.2009

2.1 QPRF author and contact details:

SIEF-IT Partner

3. Prediction

Endpoint (OECD Principle 1)

a. Endpoint:

Human health effects. Eye irritation/corrosion

b. Dependent variable:

log (MMAS/P°)

3.2 Algorithm (OECD Principle 2)

a. Model or submodel name:

QSAR model for Eye irritation (Draize test)

b. Model version:

30.01.2009

c. Reference to QMRF:

The corresponding QMRF named "QSAR model for Eye irritation (Draize test)" has been newly compiled.

d. Predicted value (model result):

SP = -4.21

e. Predicted value (comments):

MMAS/P° = 6.17 $x10^{-05}$

f. Input for prediction:

Mol file, as shown in 1.5

g. Descriptor values:

Gravitation index (all bonds) (AM1)	147.21
Max nucleophilic reactivity index (AM1) for C atoms	7.43E-003
Lowest e-e repulsion (1-center) (AM1)	2.79
HASA-1/TMSA (AM1)	0.37

3.3 Applicability domain (OECD principle 3)

a. Domains:

i. *descriptor domain*

Almost all descriptor values for formaldehyde fall in the applicability domain (training set value ±30%). The exception is the value of HASA-1/TMSA (AM1) that is exceptionally large (about 150% of the largest value in training set) due to the small size (and, hence, TMSA)

of the molecule. However, this is expected behaviour and this value may still be considered acceptable.

ii. *structural fragment domain*

Formaldehyde is structurally similar to the training set compounds

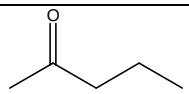
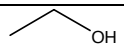
iii. *mechanism domain*

Formaldehyde is considered to be in the same mechanistic domain as the molecules in the training set.

iv. *metabolic domain, if relevant*

n/a

b. Structural analogues:

CAS	structure	smiles	source	exp. value
67-64-1		CC(=O)C	training	-3.66
107-87-9		CCCC(=O)C	training	-4.05
64-17-5		CCO	training	-3.51

c. Considerations on structural analogues:

The eye irritation values for small alcohols and ketones fall in the same range as the predicted value for formaldehyde. The structural analogues are considered to fall within the same mechanistic domain

3.4 The uncertainty of the prediction (OECD principle 4)

The training set is not from one lab but a collection. However, it has been shown to be of reasonable quality. Formaldehyde is slightly smaller than typical representatives of the training set.

3.5 The chemical and biological mechanisms according to the model underpinning the predicted result (OECD principle 5).

It has been discussed in the literature that while overall eye irritation has positive correlation with the polarity/water solubility of a compound, small and highly water soluble compounds may exhibit reduced eye irritation potency. This explains the relatively small predicted value as compared to the data of similar structures. Small hydrophilic molecules have less capability of disrupting the phospholipid structures of the membrane.