Reliability in Predictive Models under Alternative Treatments of Predictive Uncertainty
– QSPRs in Chemical Safety Assessments

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Background and aim
In the absence of experimentally tested physicochemical endpoints, European chemical regulation under REACH allows the use of non-testing strategies such as Quantitative Structure-Property Relationships (QSPR) to predict the required information using analogy models. A QSPR may be more or less reliable for predicting a property of a chemical compound. Quantitative measures of predictive reliability support the decision on whether a model is reliable enough to use for prediction. The integration of non-testing strategies into decision making calls for evaluated approaches to treat predictive uncertainty and reliability in QSPR predictions. The aim was to illustrate the practical impact of the treatment of epistemic uncertainty in QSPR predictions on decision making, by showing how the judgment of compounds as being more or less inside the applicability domain of a predictive model may transfer to the treatment of predictive uncertainty.

Conclusions
Alternative approaches to assess predictive uncertainty detects the same pattern in uncertainty and reliability (Fig 1 & 4), but has an impact on the reliability in a model prediction and thereby the judgment on whether a compound is inside the applicability domain (Fig 2), since the treatment of predictive uncertainty

- forces us to balance predictive reliability to precision (Fig 2)
- reflect our preferences/aversion to uncertainty in the predictions (Fig 3 & 4)

Treatment of epistemic uncertainty depend on the kind of background knowledge and context, here the replacement of experimental data by non-testing information through analogy predictions in chemical regulation.

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