

Strengthening Regulatory (Q)SAR Evaluation: Application of the (Q)SAR Assessment Framework to a Bioaccumulation Case Study

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INTRODUCTION

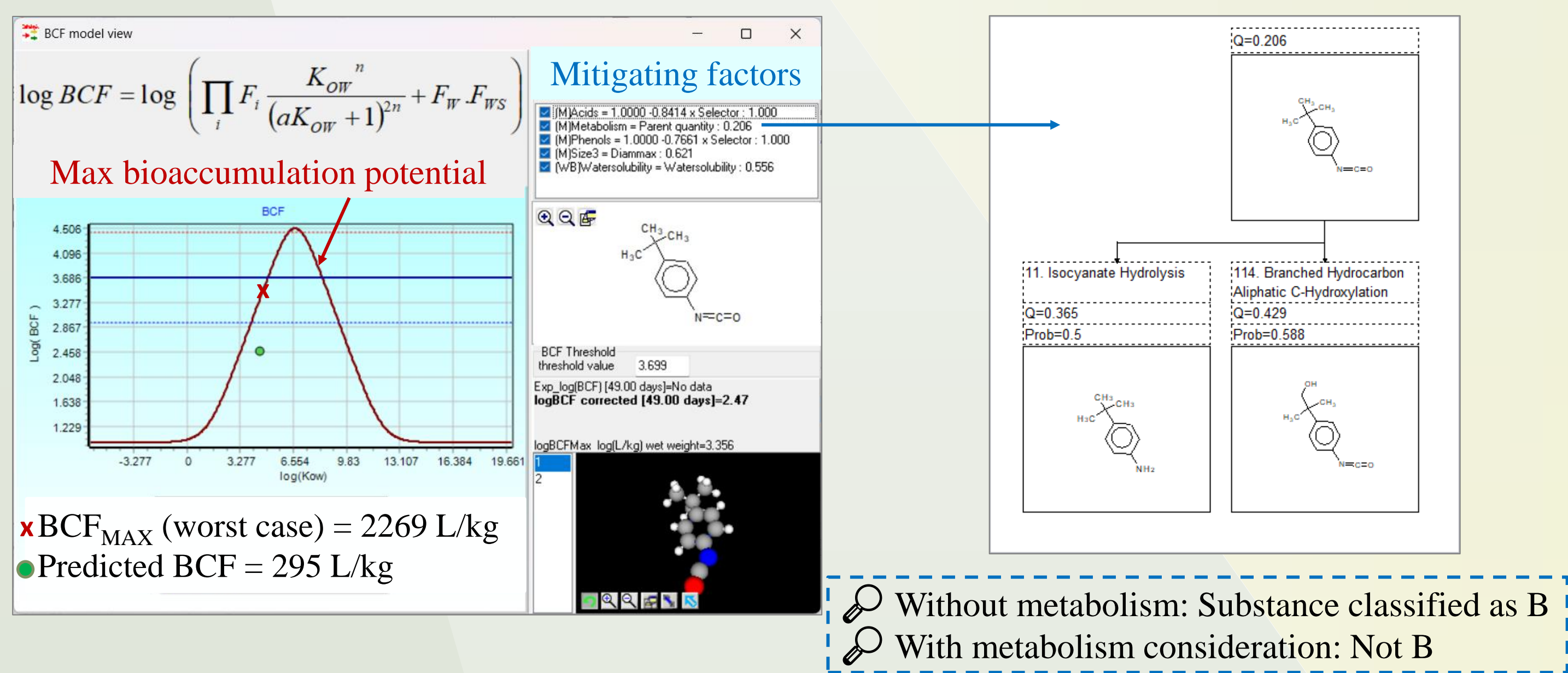
The growing use of *in silico* Quantitative Structure–Activity Relationship ((Q)SAR) methods offers major opportunities to strengthen regulatory chemical assessments and reduce reliance on animal testing. However, consistent and transparent evaluation of (Q)SAR predictions remains a key challenge for regulatory acceptance. The (Q)SAR Assessment Framework (QAF) addresses this by providing practical, harmonized guidance for evaluating models and predictions across regulatory contexts, building on internationally recognized principles such as the OECD (Q)SAR validation principles.

A bioaccumulation case study is used to demonstrate the QAF application from a user's perspective in the context of REACH registration.

CASE STUDY

Substance: 4-*tert*-Butylphenyl isocyanate, CAS 1943-67-5

Results: CATALOGIC BCF base-line model [1]



QSAR ASSESSMENT FRAMEWORK (QAF)

Regulatory Challenges

- Inconsistent reporting
- Limited transparency
- Reviewer uncertainty

QAF Solution

- Harmonized evaluation criteria
- Standardized QPRF/QMRF
- Structured reliability assessment

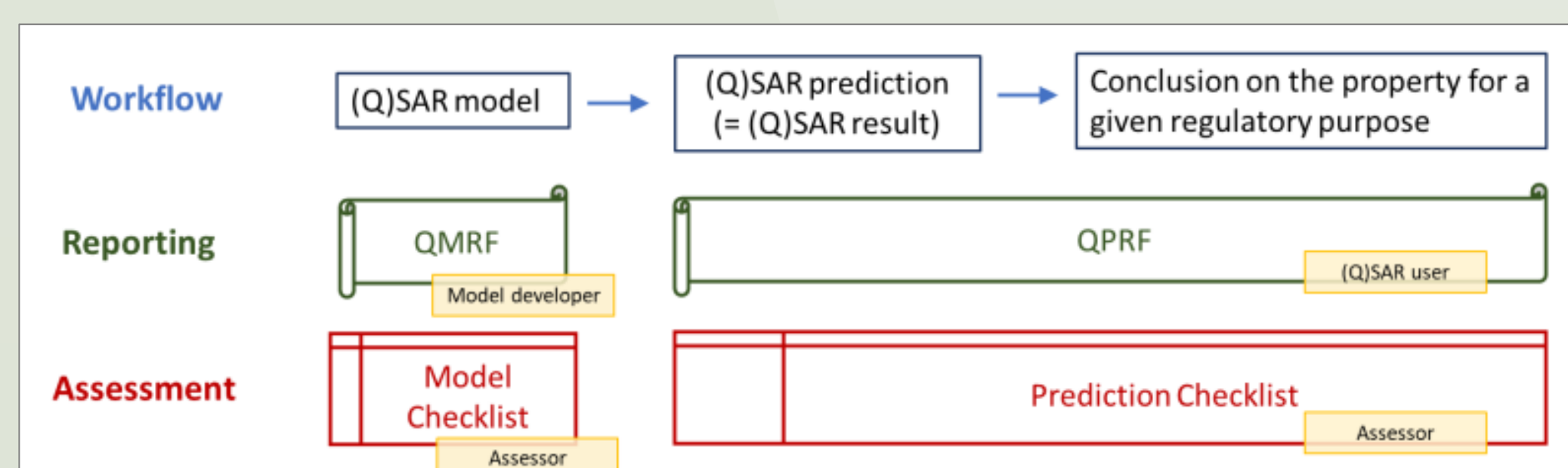


Fig. 1. (Q)SAR Assessment Framework (QAF) result based on an individual prediction [2]

(Q)SAR MODEL REPORTING FORMAT (QMRF)

IN ACCORDANCE WITH QAF

All QMRF documents for the CATALOGIC software models are updated and aligned with the structure and terminology defined in the new QMRF template proposed by QAF [2]. The QMRFs are associated with the five OECD principles for the validation of the (Q)SAR models:

- endpoint definition,
- algorithm,
- validation statistics,
- applicability domain, and
- mechanistic interpretation

but including additional descriptions for some of the specific fields as requested by the QAF documentation.

Table 1 illustrates the compliance of the BCF base-line model with these principles.

#	OECD (Q)SAR validation principles	QMRF sections of the BCF base-line model	Fulfilled
1	A defined endpoint	Section 3. Defining the endpoint – OECD Principle 1	Yes
2	An unambiguous algorithm	Section 4. Defining the algorithm – OECD Principle 2	Yes
3	A defined domain of applicability	Section 5. Defining the applicability domain of the model – OECD Principle 3	Yes
4	Appropriate measures of goodness-of-fit, robustness and predictivity	Section 6. Defining goodness-of-fit and robustness (internal validation) – OECD Principle 4	Yes
5	A mechanistic interpretation if possible	Section 8. Providing a mechanistic interpretation – OECD Principle 5	Yes

Table 1: Compliance of the BCF base-line model with OECD (Q)SAR Validation Principles

References:

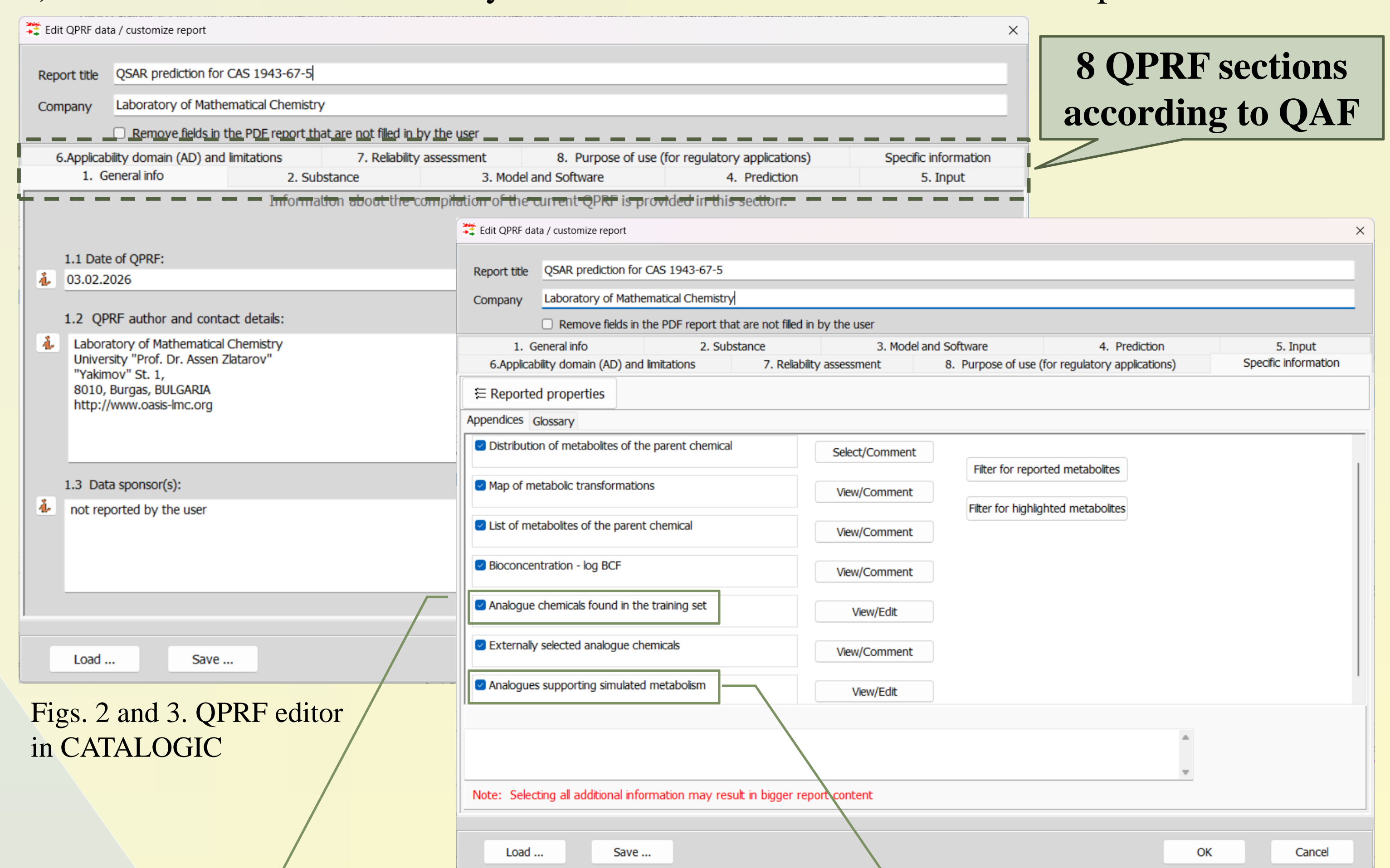
- [1] Dimitrov et al., *SAR QSAR Environ Res.*, **2012**, 23(1-2):17-36
 [2] OECD. OECD Series on Testing and Assessment No. 405, **2024**.

(Q)SAR PREDICTION REPORTING FORMAT (QPRF)

IN ACCORDANCE WITH QAF

The QPRF editor available for any prediction done by the CATALOGIC software models, is updated to include all sections and information requested by the new QPRF template proposed by QAF [2].

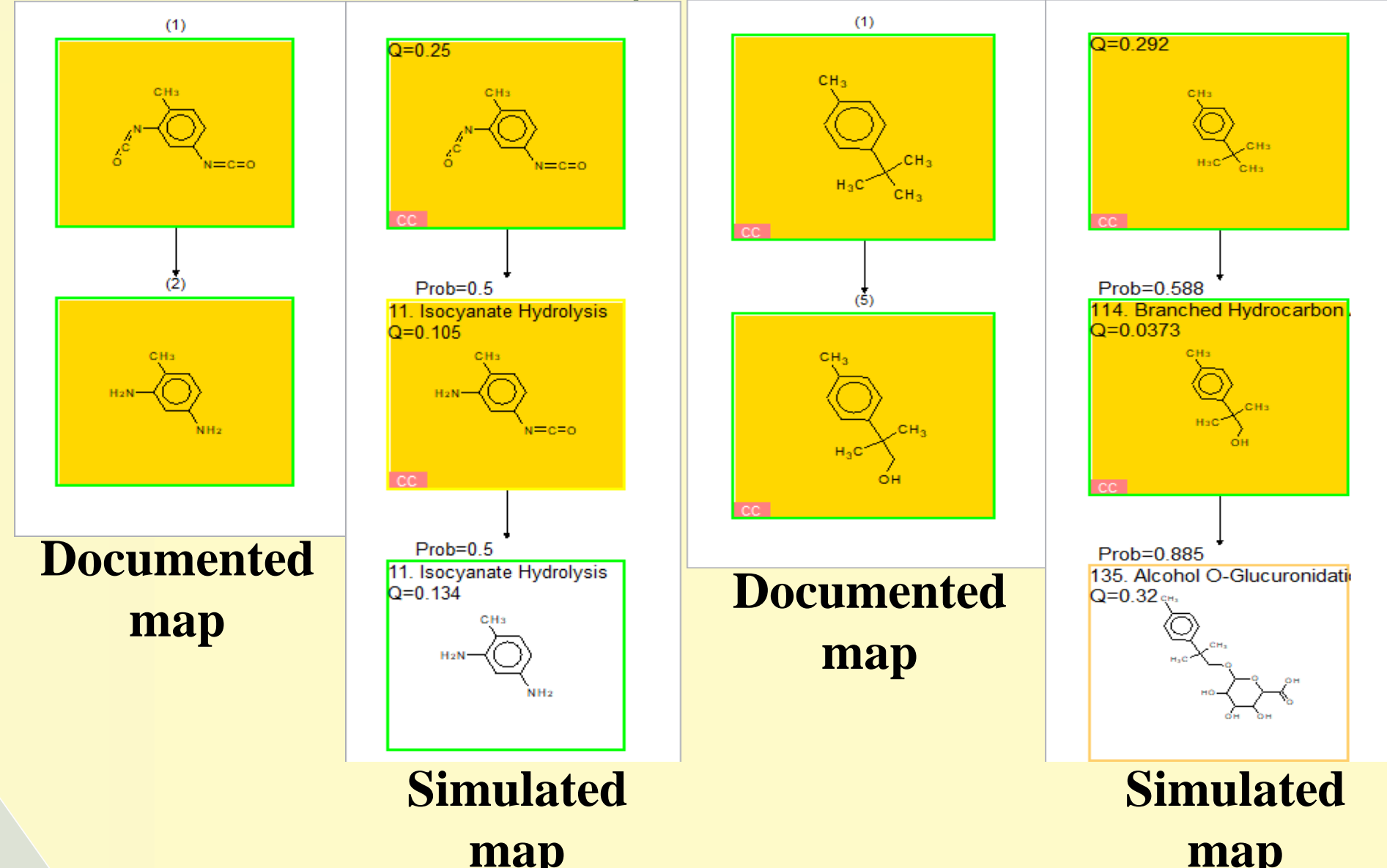
The prediction results for the target chemical (CAS 1943-67-5) generated with the BCF base-line model along with the additional support found using the available software tools are automatically populated in the respective fields of the QPRF editor (Fig. 2 and 3). The user can further modify or add other details/comments on the prediction.



Analogues supporting prediction

CAS 25567-40-2	CAS 584-84-9
Exp BCF 2.87 log (L/kg)	Exp BCF 2.28 log (L/kg)
Source: ExxonMobil	Source: NITE, Japan

Analogues supporting simulated metabolism



EXPORTING RESULTS TO IUCLID6 ACCORDING TO QAF

- 17 new QAF-related fields added to the OECD Harmonized Templates in IUCLID6
- Direct connection between CATALOGIC and IUCLID6 allows an automated population of the QAF fields when export CATALOGIC predictions to IUCLID6
- Completed QPRF report automatically appears as an attachment

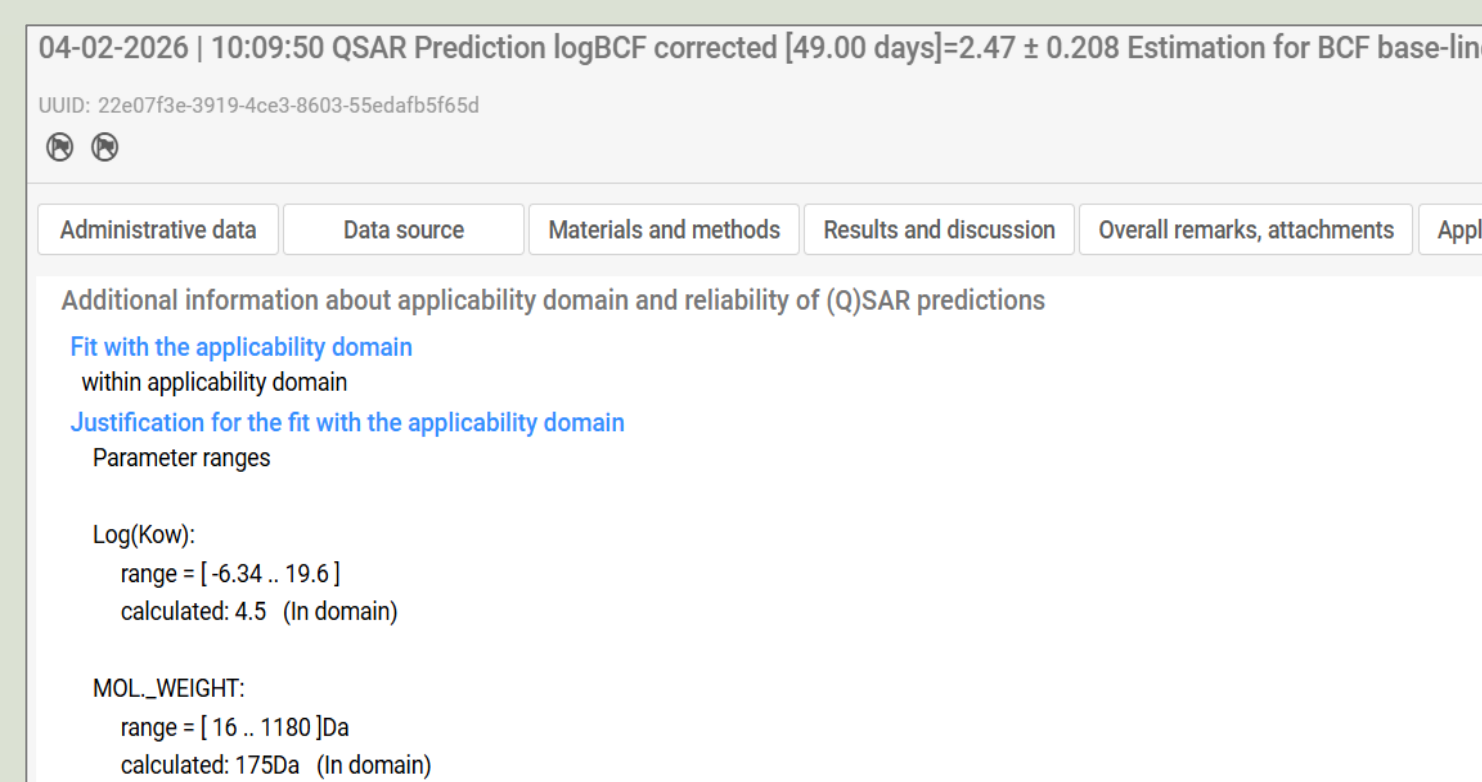


Fig. 4. Applicability domain assessment in IUCLID6

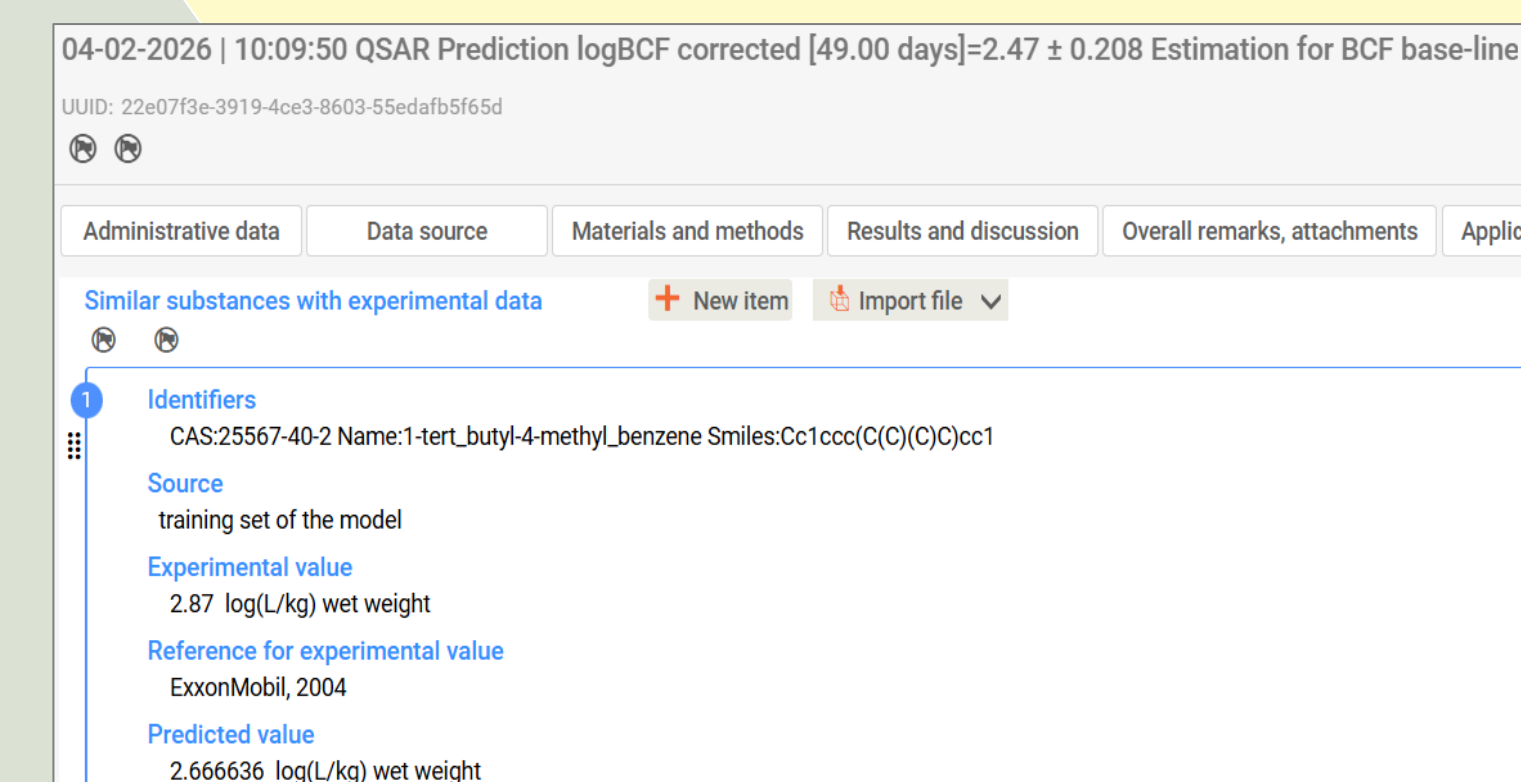


Fig. 5. Similar substances report in IUCLID6

CONCLUSIONS

- QAF strengthens regulatory confidence in (Q)SAR methods and supports wider acceptance of non-animal approaches by enhancing transparency and standardization through updated QMRF and QPRF templates.
- The CATALOGIC software models includes not only the updated QMRF and QPRF templates but also provides automated population on most of the fields proposed by QAF, which facilitates the users' work.
- The direct export to IUCLID6 enhances regulatory workflow efficiency.

