

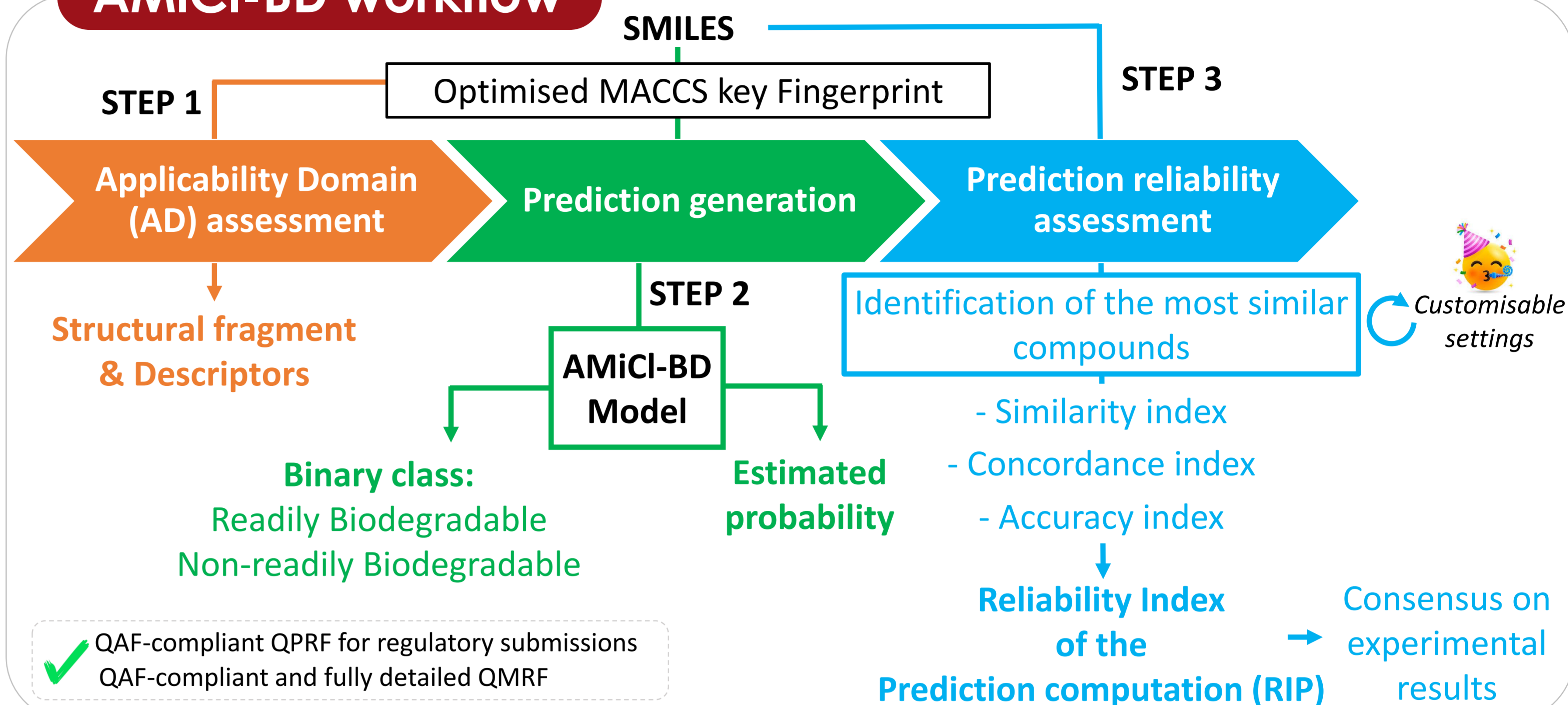
Introduction

Aerobic microbial biodegradation of organic chemicals is a key environmental process mandatory for the Persistence Bioaccumulation Toxicity (PBT) triad in various regulatory frameworks. The **OECD 301/310 Guidelines** (OECD, 1992&2014)^[1,2] set out the criteria to experimentally determine if a chemical is readily biodegradable (RB), meaning that at least 60% mineralisation occurs within 28 days, meeting the 10-day window. Several models used for regulatory purposes predict this endpoint but, depending on the model, the statistics are not satisfactory enough or the provided information from the software or the QMRF, if existing, may be barely sufficient to edit **QSAR Assessment Framework**-compliant documents. Thus, KREATIS has developed the **Aerobic Microbial Classification of BioDegradation (AMiCI-BD)** model which is based on **high-accuracy curation and data validation**, on mechanistic understanding and on good-practice modeling and which aims to meet the authorities' expectations. This poster introduces this new model and compares its performance against that of a set of models regularly used for regulatory purposes and recently published by ECHA^[3].

A 5 OECD principle compliant model

- Principle 1: a defined endpoint**
Ready biodegradability (OECD301/310).
Studies selected from a drastic 3 steps curation workflow
- Principle 2: an unambiguous algorithm**
Random Forest (RF) or Support Vector Machine (SVM)
- Principle 3: a defined domain of applicability (AD)**
Applicability Domain (descriptor, structure) and a dynamic Reliability Index of the Prediction computation.
- Principle 4: Appropriate measures of goodness of fit, robustness and predictivity**
Very good goodness-of-fit, robustness and predictivity results.
- Principle 5: Mechanistic interpretation**
Provided from genetic algorithm selected features and random forest selected metrics.

AMiCI-BD workflow



Performance comparison

ECHA compared model performance from REACH regulation chemicals^[3]. The predictive statistics values presented below come from this article, with the exclusive addition of AMiCI-BD model performance. AMiCI-BD statistics were strictly computed as mentioned in the ECHA article: training and validation set chemicals were removed; 2/ the applicability domain was assessed, and the reliability index was computed by default, as defined in QMRF (settings not customized).

| | BIOWIN 3 ^[4] | BIOWIN 5 ^[5] | OPERA ^[6] | VEGA ^[7] | CATALOGIC ^[8] | AMiCI-BD RF | | AMiCI-BD SVM | |
|-----------------------------|-------------------------|-------------------------|----------------------|---------------------|--------------------------|-------------|------|--------------|------|
| Number of chemicals | 2655 | 2418 | 2310 | 2288 | 2316 | 1946 | | | |
| % of chemical in AD | 79* | 91* | 68* | 28* | 56* | 36* | 24** | 38* | 31** |
| Sensitivity (NRB) | 22 | 79 | 62 | 59 | 85 | 79 | 84 | 76 | 85 |
| Specificity (RB) | 98 | 68 | 81 | 96 | 56 | 88 | 94 | 88 | 92 |
| Balanced accuracy | 60 | 73 | 71 | 77 | 71 | 84 | 89 | 82 | 89 |
| Positive predictivity (NRB) | 97 | 88 | 88 | 95 | 77 | 93 | 97 | 93 | 96 |
| Negative predictivity (RB) | 34 | 52 | 49 | 62 | 68 | 68 | 74 | 65 | 75 |

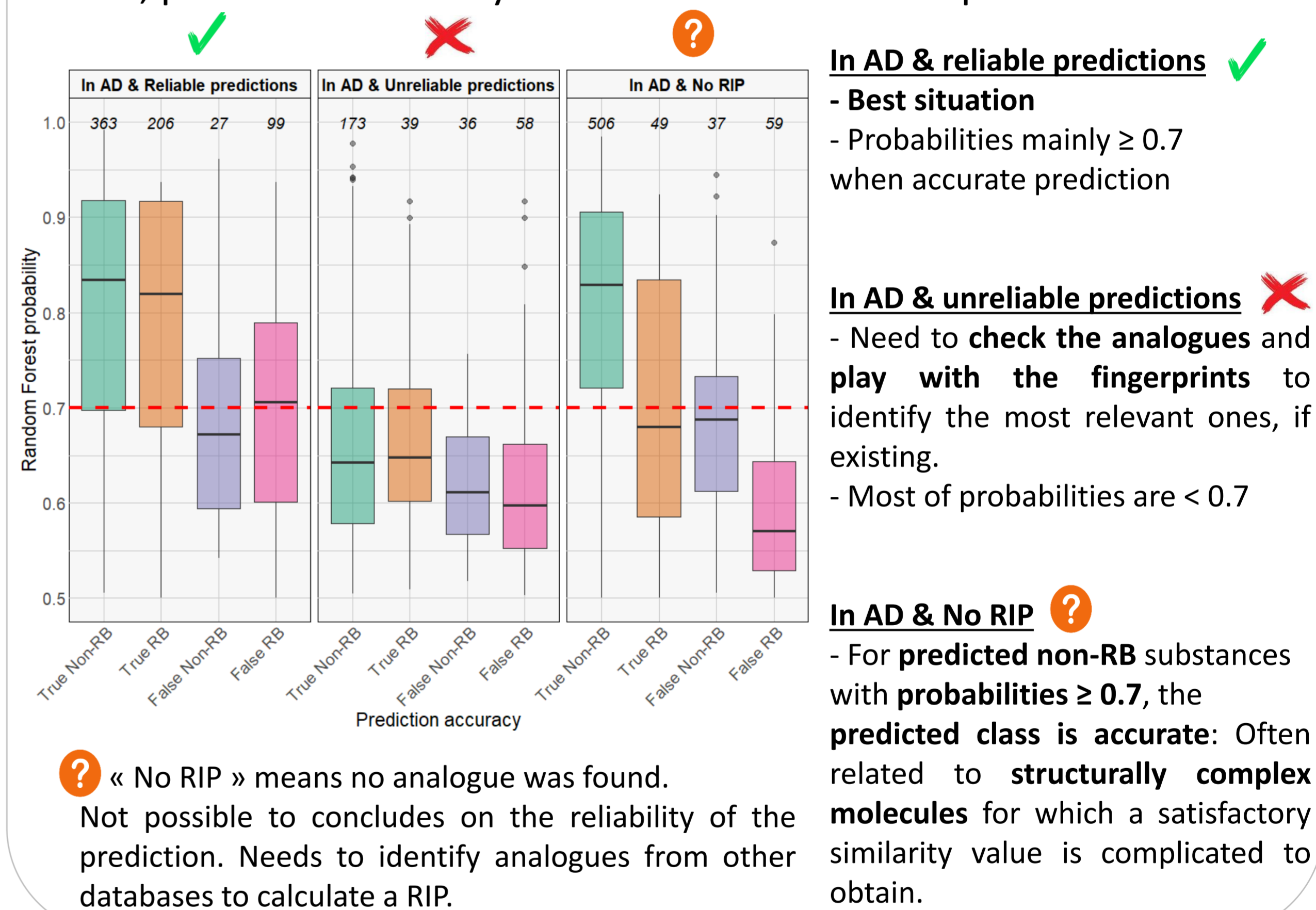
- AMiCI-BD models display:
 - One of the **best capacity to detect the true RB compounds**,
 - More importantly, **classifies less non-RB compounds as RB than the others (more precise)**,
 - **Balanced accuracy is also the best. A lot of compounds were withdrawn because of no RIP!**
- Negative predictivity remains the lowest performing metric for many models (data issue due to regulatory threshold in modelling? Microbial ecology influence? Let's discuss this)

* In model applicability domain as defined in Karamertzanis et al., (2026); AMiCI-BD: In AD & RIP ≥ 0.7 (from top two analogues)

** In AD & RIP ≥ 0.7 & probability ≥ 0.7

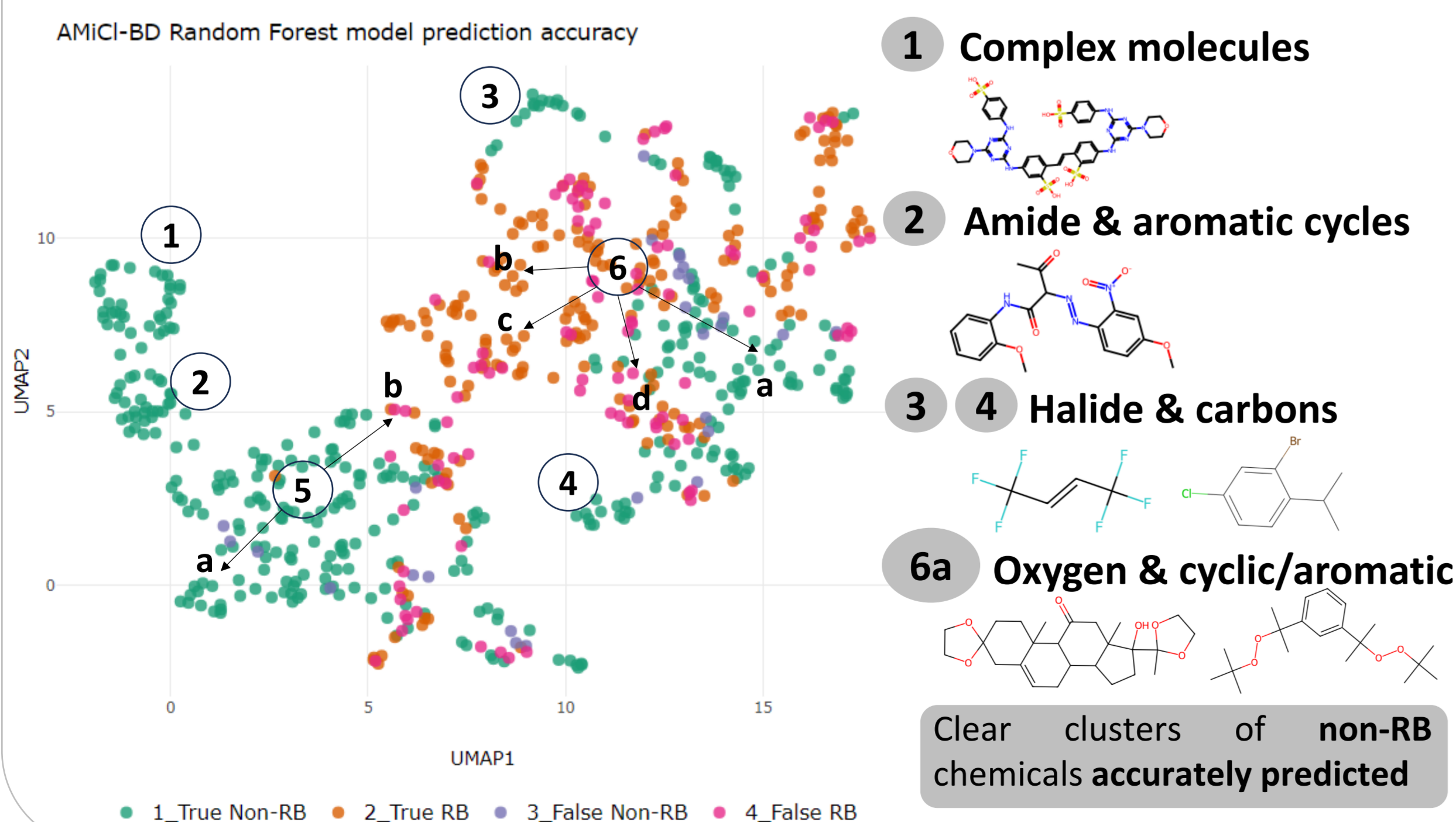
Going further: Relying on probabilities?

AMiCI-BD models provide an **AD assessment**, a **RIP value** and a **probability**. The probability is related to the trees for the RF and to the distance between the RB and Non-RB clusters separation for the SVM. Below, prediction accuracy was related to RF model probabilities.



AMiCI-BD accuracy exploration

- Each point represents one substance from Karamertzanis et al. (2026), external to the AMiCI-BD model training and validation sets
- UMAP based on the 166 bits of MACCS key fingerprint
- Each substance falls within the model AD and has a RIP value ≥ 0.7



5a Cyclic amines
5b Linear amines
Big « amine based » cluster (5) mostly related to non-RB chemicals. Discrepancies occur mostly for linear molecules. No clear understanding of such results based on the studies. Role of pKa in the results?

6b Oxygen based
6c Oxygen & aromatic
Experimental RB and Non-RB chemicals overlap mostly in the « oxygen based » cluster (6). Structural moiety, % of degradation close to 60% at 28 days and wrong interpretation mostly explain this overlap. This mainly happens in RB dominant chemical space and is due to experimental negative bias and strict regulatory threshold -> issues to detect true RB.

Conclusion

AMiCI-BD is not just another model : - Best performance to accurately identify RB compounds and presents the **best balance accuracy**, for a REACH substance dataset. - Relying on **AD, RIP and probabilities** supports the confidence in the prediction. - **Precision on True RB is the trickiest point**: Overlap of non-RB chemicals in the same space (here, oxygen and nitrogen-based compounds). Serious data validation especially mandatory for such compounds as the model predicts from what it learns.

REFERENCES

¹OECD (1992), *Test No. 301: Ready Biodegradability*, OECD Guidelines for the Testing of Chemicals, Section 3, OECD Publishing, Paris, <https://doi.org/10.1787/9789264070349-en>; ²OECD (2014), *Test No. 310: Ready Biodegradability - CO2 in sealed vessels (Headspace Test)*, OECD Guidelines for the Testing of Chemicals, Section 3, OECD Publishing, Paris; ³Karamertzanis P.G., Ekholm H., Yli-Tuomola A., Cesnaitis, R. Andreou K., Nyman A.M., De Coen W. (2026). A comparative assessment of predictive methods for ready biodegradation using REACH experimental data. *Computational Toxicology* 37, 100398; ⁴Boethling, R.S., Howard P.H., Meylan W., Stiteler W., Beauman J., Tirado N. (1994) Group contribution method for predicting probability and rate of aerobic biodegradation. *Environ. Sci. Technol.* 28 (3) 459–465; ⁵Tunkel J., Howard P.H., Boethling R.S., Stiteler W., Loonen H. (2000) Predicting ready biodegradability in the Japanese ministry of international trade and industry test. *Environ. Toxicol. Chem.* 19 (10) 2478–2485; ⁶Mansouri K., Grulke C.M., Judson R.S., Williams A.J. (2018) OPERA models for predicting physicochemical properties and environmental fate endpoints. *J. Cheminform.* 10 (1) 1–19; ⁷Lombardo A., Pizzo F., Benfenati E., Manganaro A., Ferrari T., Gini G. (2014) A new in silico classification model for ready biodegradability, based on molecular fragments. *Chemosphere* 108, 10–16; ⁸Dimitrov S., Pavlov T., Dimitrova N., Georgieva D., Nedelcheva D., Kesova A., Vasilev R., Mekenyan O. (2011). Simulation of chemical metabolism for fate and hazard assessment. II CATALOGIC simulation of abiotic and microbial degradation, *SAR QSAR Environ. Res.* 22 (7–8).



Scan QR code to download the poster