

Ecotoxicity Testing of UVCBs

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INTRODUCTION

Testing of UVCBs poses a regulatory challenge and especially so when the accent is on the “U” for Unknown as well as “V” for Variable as is often the case for botanical extractions. Certain categories of Natural Complex Substances (NCS2) present multiple complexities for regulatory dossier submission:

- Only a small fraction of the mixture has been identified and may contain hundreds of constituents;
- Constituent concentrations may vary according to batch and quality;
- They may have high viscosity, high volatility, low solubility and/or hydrophobicity;
- They may be toxic, but it is unknown which constituents are responsible.

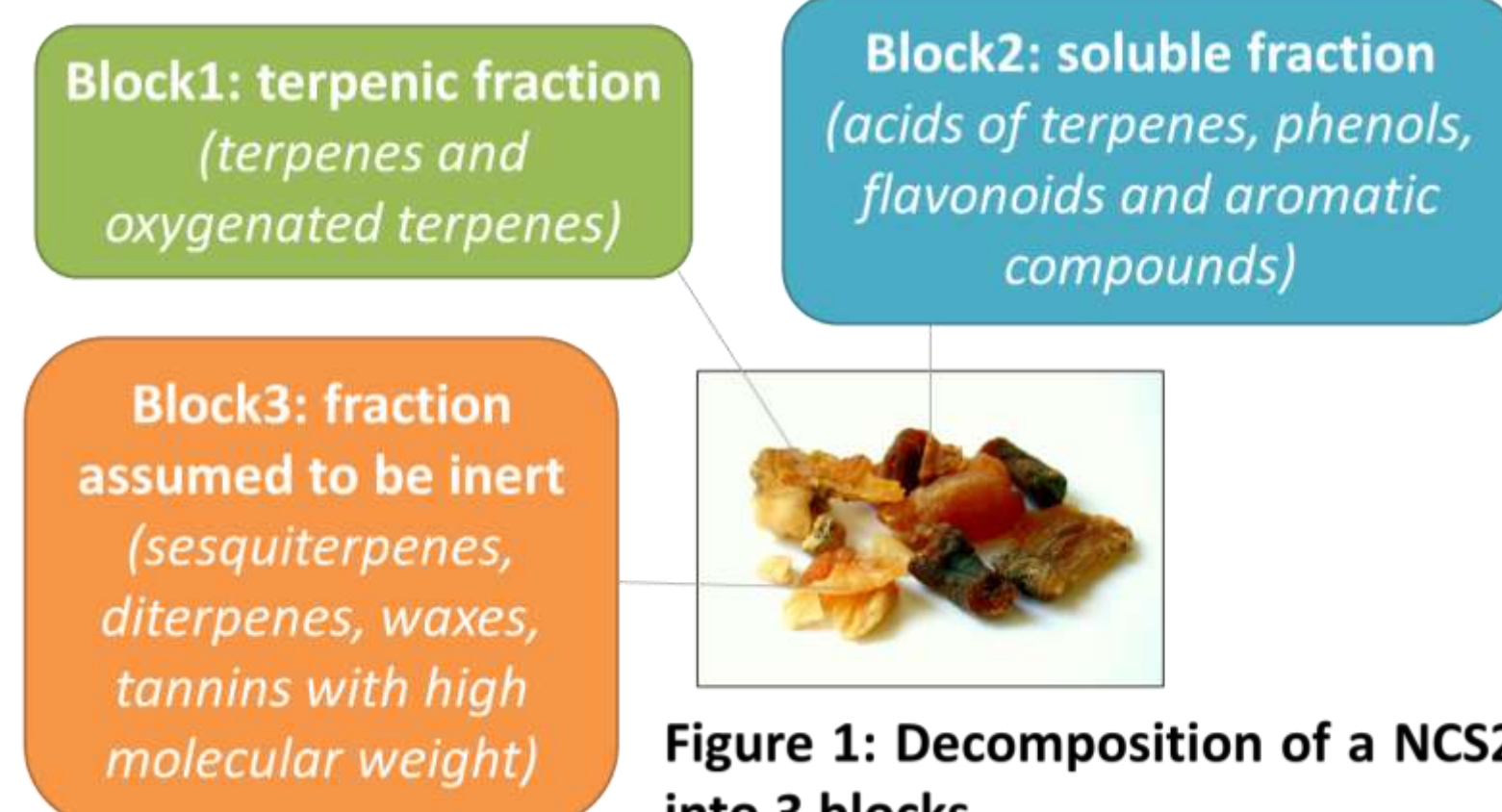
The CHANCES2 project started in October 2020 and aims to provide an experimental methodology supported by *in silico* modelling in order to test, mechanistically explain and predict aquatic toxicity of NCS2. In this project we aim to find the optimal strategy between laboratory testing using chemical analysis to ecotoxicity profile and *in silico* modelling the laboratory results.

- ⇒ Can we mechanistically understand, determine and predict the toxicity of a natural complex mixture that is <50% analysable?
- ⇒ And if we can do it once, then can we do it for 100s of other complex substances?

NCS2-ADAPTED METHODOLOGY

Substances are tested whole and are split into three fractions. The fractions are defined as follows:

1. Terpenic/volatile: high % of profile analysable
2. Soluble/non-volatile: moderate % analysable
3. Inert: negligible % analysable,



Hypotheses to be tested:

- 1) The toxicity of the **fraction 1** can be accurately modelled *in silico* using the iSafeRat® WAF model;
- 2) The critical constituents of the **fraction 2** can be analytically elucidated ;
- 3) The toxicity of the **fraction 2** to daphnids and algae can be measured;
- 4) **Fraction 3** is expected not to be toxic in a chronic daphnid limit test
- 5) The results of the analytical and toxicity results of these three fractions can be summed (using an *in silico* chemical activity approach) to obtain the same toxicity result as that found for the whole NCS2 substance.

A project on partially unknown complex mixtures using mechanistic justification to obtain meaningful aquatic ecotoxicity results

CHANCES2

Compartmentalised Hazard Assessment for Natural Complex Extracted Substances (Type 2)

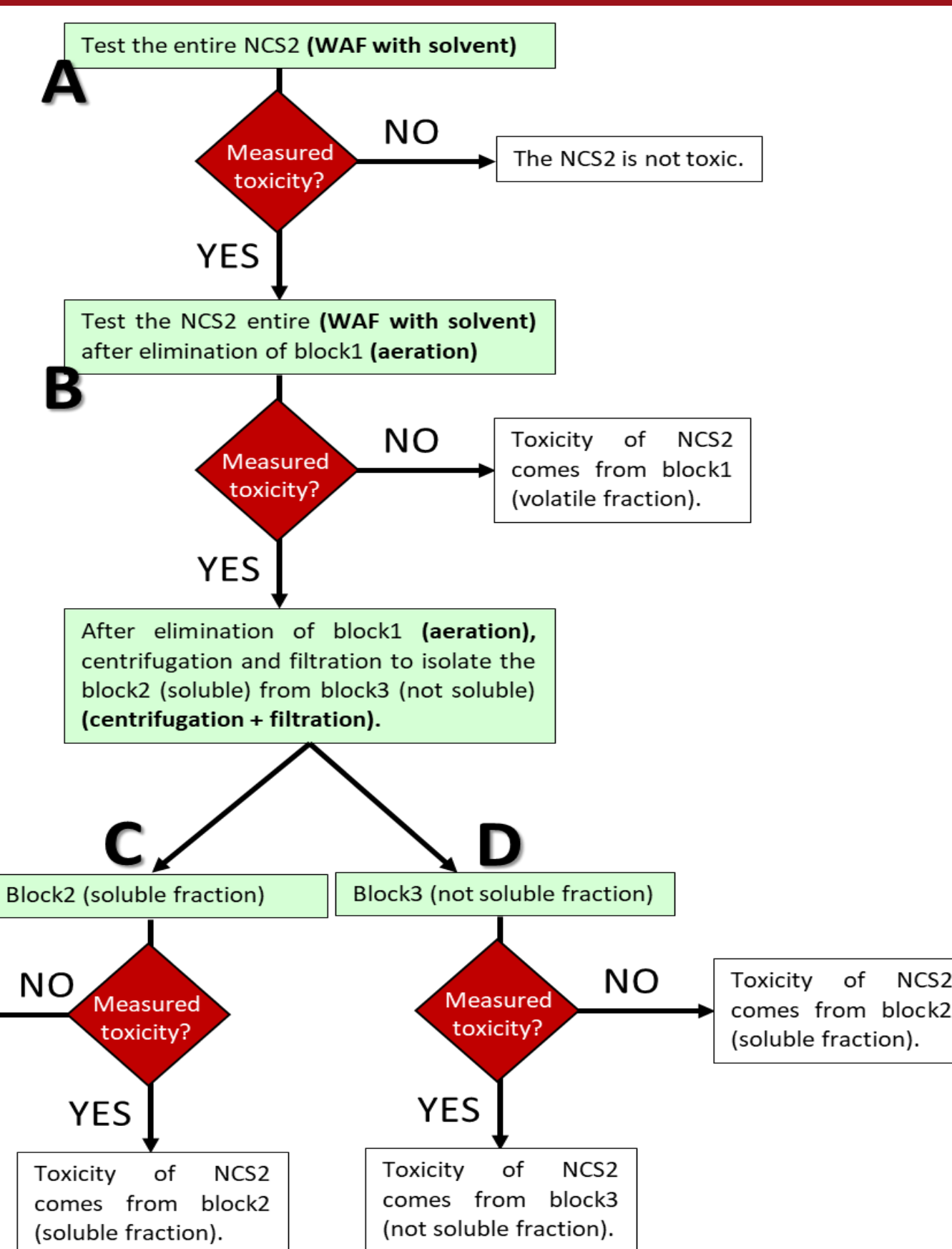


Figure 2: Scheme outlining the testing methodology to determine the relative toxicity of the whole substance and the 3 fractions.

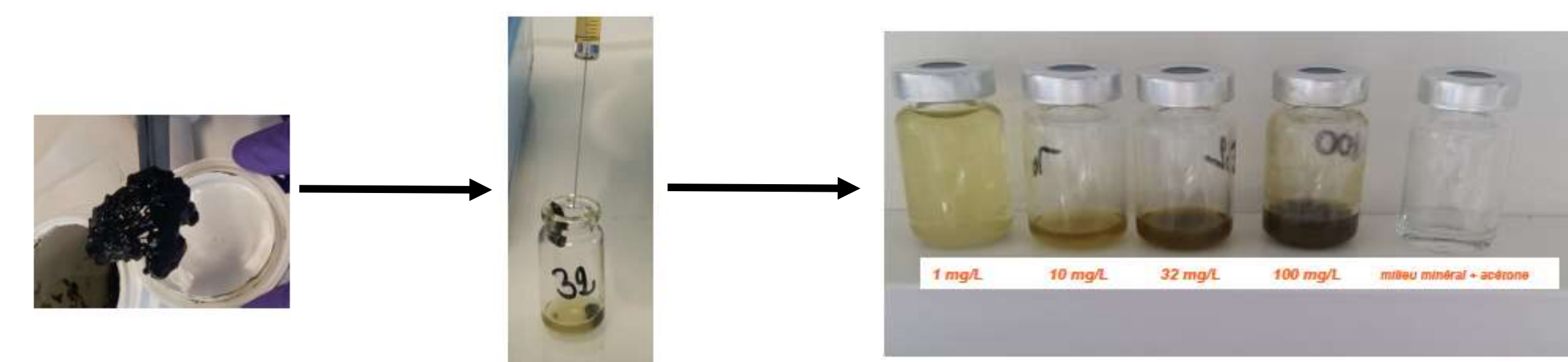


Figure 3: A typical NCS2 substance dispersed in a solvent prior to preparation of loading rates for WAF testing in the lab.

CURRENT SITUATION

The CHANCES2 project is underway with the fractionation of the substances being undertaken at university of Côte d'Azur.

Next steps:

- Preliminary ecotoxicity testing and *in silico* WAF calculations
- Final results of first substance expected end of 2021

This project is sponsored by RIFM

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