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1) Introduction

Extraction methods can vary greatly in their efficiency to extract so-called *incurred residues* that form when plant protection products are applied to agricultural crops. Active substances and their metabolites can be incorporated into food or feed crops, and thus may occur in tissues and animal products. Notably, the use of an analytical method with poor extraction efficiency (EE) can lead to an underestimation of the actual residue levels. Investigation of EE is therefore a key data requirement for method validation for food and feed of plant and animal origin.

2) When is EE needed?

| Mandatory | Case-by-case | Not needed |
|--|--------------------------------------|---------------------------------|
| Active substance registration or renewal | Plant protection product submissions | Annex IV substances (= no MRLs) |
| | MRL applications | |

ANALYTICAL METHODS PERSPECTIVE

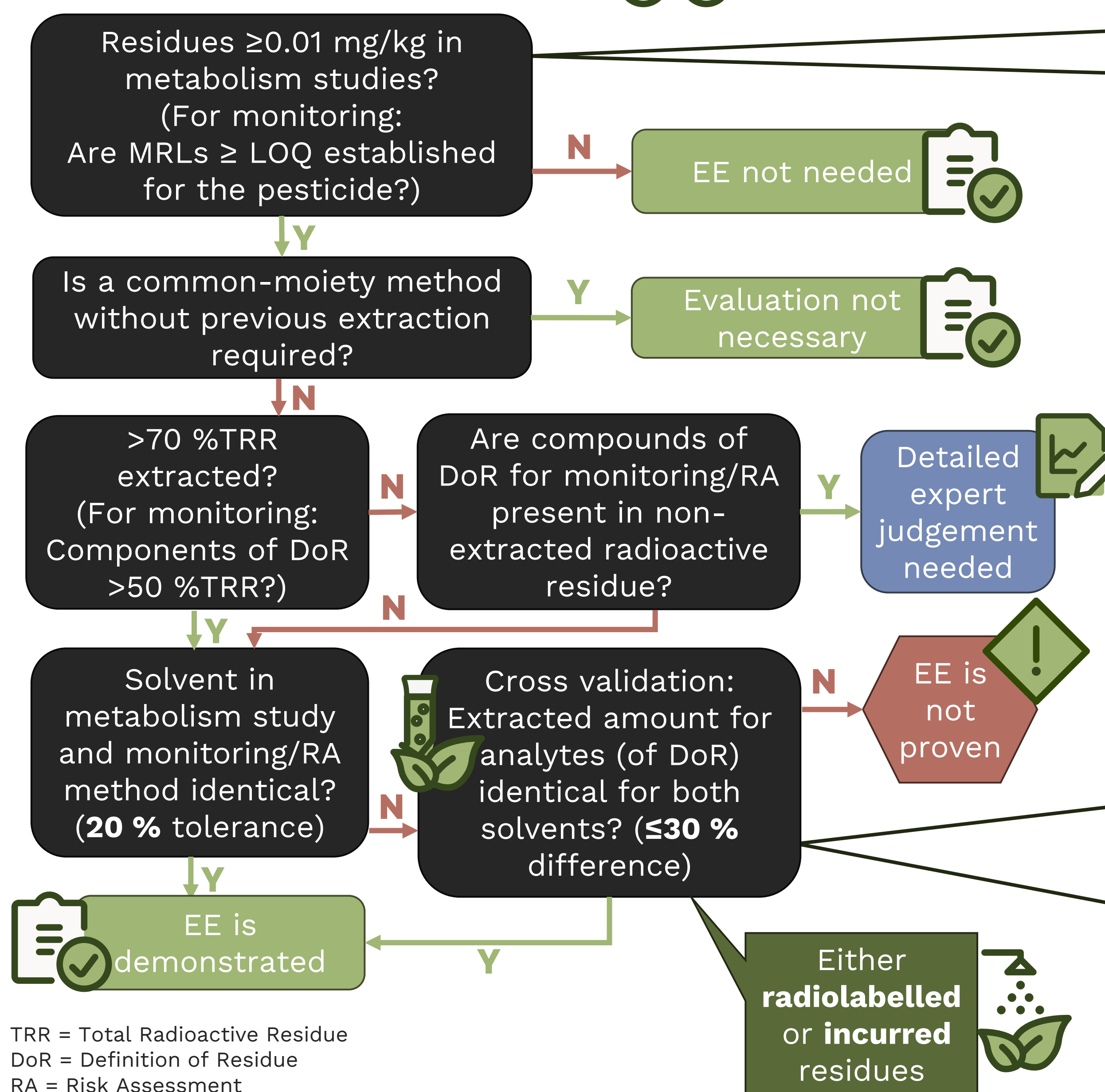
Plant matrices:

- Check surface wash experiments if **justification** is possible
- Metabolism data may not be available for each **matrix group** [compare 2,3]
- **Bridging** between high water and acidic matrices for slightly acidic matrices may be possible with justification
- **Difficult matrices** depend on the availability of suitable sample material

Animal matrices:

- No repetition of animal **feeding studies** for EE only
- **Honey** needs no proof of EE
- Missing veterinary certificates may cause issues for **cross-border transportation** of samples with incurred residues

3) Decision Tree [1]



CONSUMER SAFETY PERSPECTIVE

- EE needs to be demonstrated for commodities showing residues ≥ 0.01 mg/kg in metabolism studies **at 1N rate**
- For plants: 1N rate is the maximum annual application rate (**cGAP**)
- For animals: 1N rate is the intake estimated from the Animal Dietary Burden (**ADB**)
- Metabolism studies are often overdosed → expected residue concentrations are re-calculated using **scaling factors**
- When **planning** new metabolism studies, EE assessment should be included

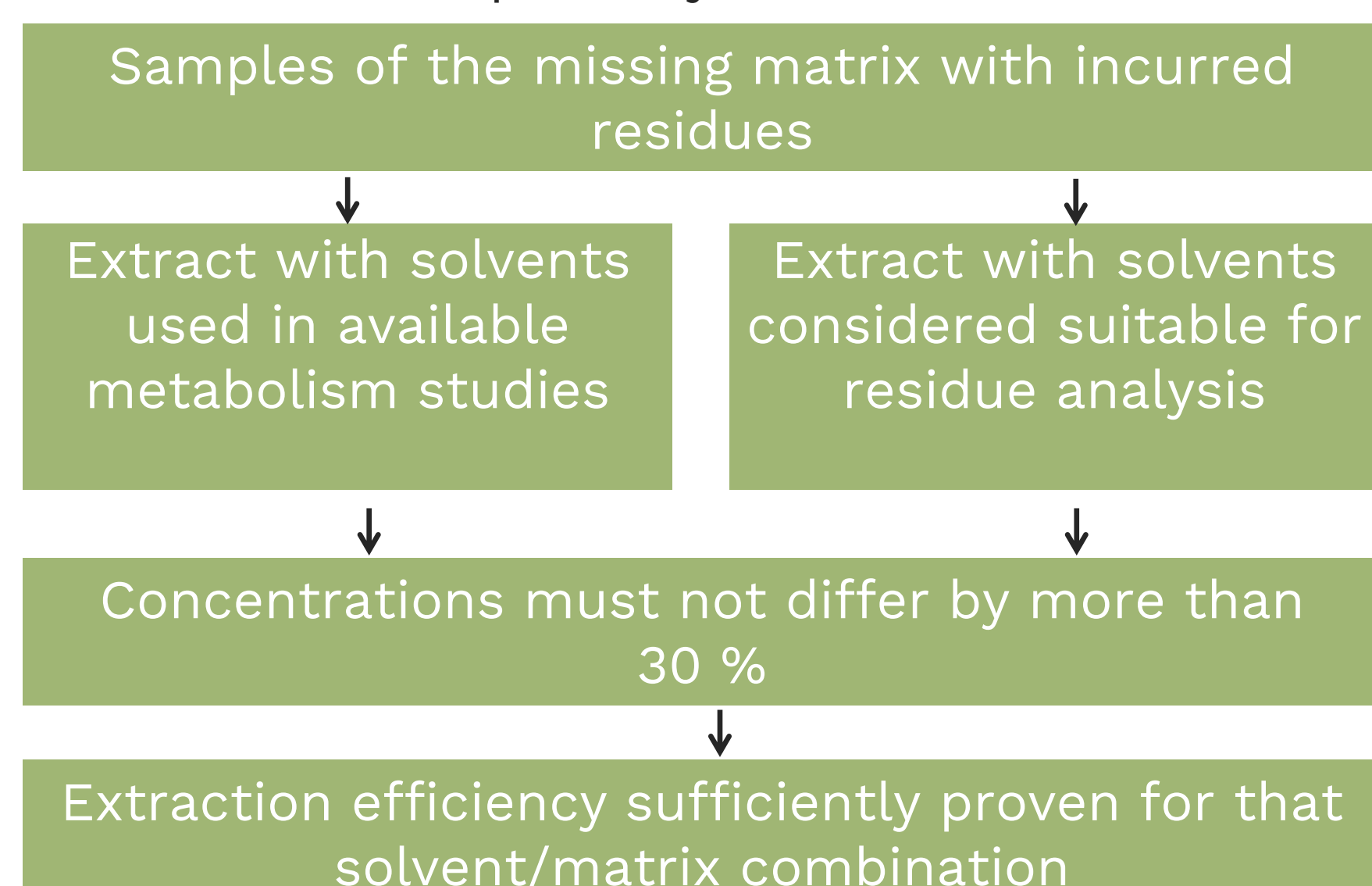
CROSS VALIDATION

- Replicate extraction **conditions** (time, temperature, agitation)
- For each method, a **validation** in accordance with SANTE/2020/12830, rev. 2 is needed
- **Pre-testing** of levels of incurred residues in test material recommended

4) No Metabolism Study with matching Matrix available? [1]

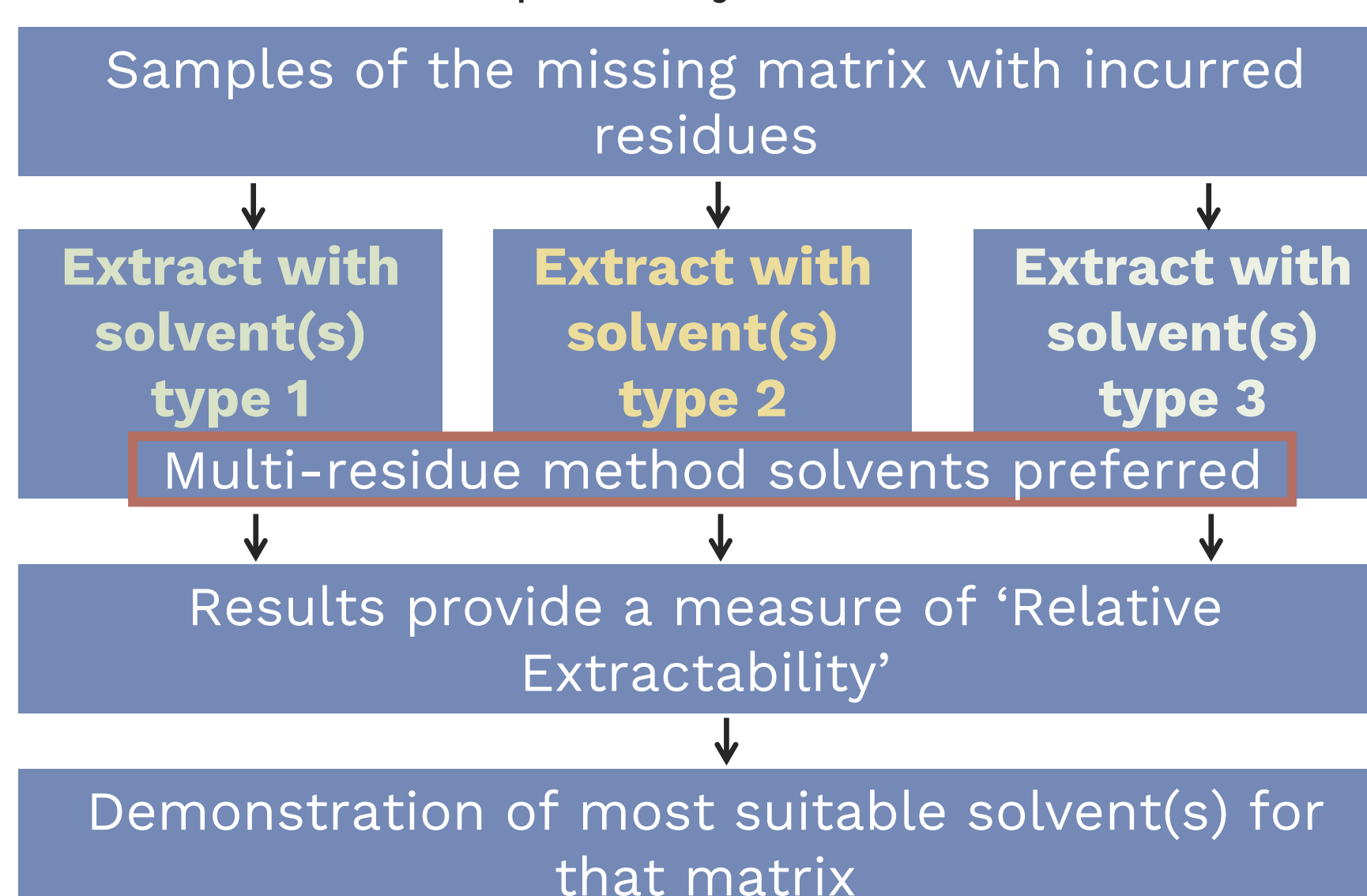
Option 1: Indirect Cross-Validation

When metabolism studies are available for crops from three analytical matrix groups. Metabolic pathways are identical.



Option 2: Relative Extractability

When metabolism studies are **not** available for crops from three analytical matrix groups. Metabolic pathways are **not** identical.



5) Take-Home Message

Extraction efficiency can become complex and thus time and cost-intensive.

Our experienced team provides all services to guide you through this jungle.

References:

- [1] SANTE/2017/10632 Rev. 5 from 11 May 2023.
- [2] OECD Guidelines for the Testing of Chemicals, Section 5, Test. No. 501: Metabolism in Crops from 25 January 2007.
- [3] SANTE/2020/12830, Rev. 2 from 14 February 2023.