**CIPAC guidelines for Multi Active Ingredient and Matrix Methods (MAIMM)  
for pesticides**

***Draft version 01 of 10 December 2017 prepared by Olivier Pigeon,  
CRA-W, Gembloux, Belgium***

1. **Introduction**

Actual CIPAC methods for determination of active ingredient identity and content in technical materials and formulated products of pesticides are applicable for only one active ingredient. These single active ingredient methods have been fully adopted by CIPAC either through full scale collaborative trials either by method extension (application of a standardized method to a different matrix or concentration range to those for which the method was originally accepted). These single CIPAC methods are actually considered as reference standard methods in many countries over the world to support registration dossiers for plant protection products and biocides and are referenced into the FAO and WHO specifications for pesticides to allow their quality control.

Due to the huge number of active ingredients and formulations available on the market, quality control laboratories are facing difficulties in applying these single active ingredient methods, which require different extraction solvents and reagents, different extraction equipment, glassware and conditions, different chromatographic GC or HPLC columns and conditions, different calibration procedures (single point calibration or calibration curve, external or internal calibration). Quality control laboratories are more and more using Multi Active Ingredient and Matrix Methods (MAIMM) which offer a number of advantages compared to single active ingredient methods. Moreover several WHO specifications are now published or under development for formulated public health products containing 2 or 3 active ingredients or 1 or 2 active ingredients combined with a synergist (e.g. long-lasting insecticidal mosquito nets and other mixture formultions for vector control). The use of Multi Active Ingredient and Matrix Methods (MAIMM) for such formulated product will greatly facilitate their quality control.

This document provides guidance for the adoption by CIPAC of Multi Active Ingredient and Matrix Methods (MAIMM) for plant protection products and biocides.

1. **Advantages of Multi Active Ingredient and Matrix Methods (MAIMM)**

The advantages for quality control laboratories of using Multi Active Ingredient and Matrix Methods (MAIMM) are summarized hereafter :

* Minimisation of the number of solvents, reagents, internal standards, extraction equipment and glassware and chromatographic columns to be used by laboratories.
* Minimisation of the changes over time from one sample to the next.
* Common extraction, chromatographic and calibration conditions applicable to the majority of active ingredients and formulations.

And associated with this :

* A significant reduction of the time needed to perform the analysis.
* A minimisation of the analytical errors or mistakes.
* A more efficient use of laboratory human, equipment and consumable resources.
* A significant reduction of the cost of the analysis.
* A faster quality control of products.

1. **CIPAC procedure for Multi Active Ingredient and Matrix Methods (MAIMM)**

**3.1 Design of Multi Active Ingredient and Matrix Methods (MAIMM)**

When developing Multi Active Ingredient and Matrix Methods (MAIMM), laboratories should consider the following points:

* The scope of the method in term of active ingredients and formulation types which are covered should be clearly defined.
* The method should minimise variations in laboratory sampling, extraction conditions of active ingredients and chromatographic analysis, and should be based on a common procedure for most of the steps involved from laboratory sampling until calculation of results.
* Nevertheless laboratory sampling and extraction conditions may depend on the formulation type or on the physical-chemical properties of the active ingredients (polarity, solubility in water and organic solvents, octanol / water partition coefficient, hydrolysis and photolysis characteristics …).
* Capillary gas chromatopraphy with flame ionisation detection (GC-FID) and high performance or ultra high performance liquid chromatography (HPLC-UV or UHPLC-UV) should be the preferred chromatographic techniques. The selection of GC or HPLC depends on the physical-chemical properties of the active ingredients.
* Basic common chromatographic conditions for GC-FID analysis should be specified such as : injection parameters (injection mode and liner, temperature, split flow, split ratio, injection volume …), column type (stationary phase), dimension and film thickness avoiding endorsing commercial products, oven temperature program, carrier gas and flow rate, detection parameters (temperature, make-up and detector gas flow rates ...).
* Basic common chromatographic conditions for U/HPLC-UV analysis should be specified such as : injection parameters (injection mode and volume …), column type (stationary phase), dimension and particle size avoiding endorsing commercial products, column temperature, mobile phase and flow rate and detection wavelengths.
* The equipment used should be those which are commonly available in laboratories analysing pesticides.
* The solvents and reagents should be as less toxic as possible and commonly available near consumables laboratory suppliers.

The CIPAC guidelines for the design of chromatographic analytical methods intended for CIPAC collaborative study (CIPAC/4105/R) - available at <http://www.cipac.org/images/pdf/CIPAC4105R.pdf> provide also recommendations on the design of capillary gas chromatography (GC) and high performance liquid chromatography (HPLC) methods.

**3.2 Adoption by CIPAC of Multi Active Ingredient and Matrix Methods (MAIMM)**

The following steps are recommended for the adoption by CIPAC of Multi Active Ingredient and Matrix Methods (MAIMM) :

* Internal validation in at least one laboratory according to the CIPAC guidelines on method validation to be performed in support of analytical methods for agrochemical formulations (CIPAC/4105/R) - available at <http://www.cipac.org/images/pdf/validat.pdf>
* Small-scale collaborative trial to be presented to the CIPAC Technical Meeting.
* Full-scale collaborative trial according to the CIPAC guidelines for collaborative study procedures for assessment of performance of analytical methods (CIPAC/3426) available at <http://www.cipac.org/images/pdf/study.pdf> and to be presented to the CIPAC Technical Meeting.

**3.3 Implementation of Multi Active Ingredient and Matrix Methods (MAIMM) into FAO and WHO specifications for pesticides**

The single active ingredient methods as actually published by CIPAC should continue to be referenced into the FAO and WHO specifications for pesticides. These methods are reference standard methods and should be mainly used to support registration dossiers for plant protection products and biocides. These methods can of course also be used for quality control of products. Additionally to these single active ingredient methods, Multi Active Ingredient and Matrix Methods (MAIMM), once adopted by CIPAC may also be referenced into the FAO and WHO specifications for pesticides and can be used for quality control of products. In case of any doubt concerning the active ingredient content in a technical or formulated product, the single active ingredient method remains the reference method.

🡪 To be discussed by the FAO/WHO JMPS

1. **References**

* Nicolas Mabon, Marie Baes and Olivier Pigeon, Walloon Agricultural Research Centre (CRA-W) (2017). Development of multi-pesticide / multi-matrix methods for determination of pesticides in LN and filter papers treated with IRS. CIPAC Symposium, Liège, Belgium, June 2014.
* Jim Garvey and Denis Carr, The Pesticide Control Laboratory, Ireland (2016). Multi-active methods in the formulation laboratory. CIPAC Symposium, Tokyo, Japan, June 2016.
* Nicolas Mabon and Olivier Pigeon, Walloon Agricultural Research Centre (CRA-W) (2014). Analytical strategies used to develop a multi active ingredients method for CQ of public health pesticides. CIPAC Symposium, Rome, Italy, June 2017.

🡪 To be completed with any other reference paper or communication