Reference document illustrating best practices on analytical strategies and interpretation of results for the formulation analysis of plant protection products obtained during official market control

v 1.0

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I. Introduction and legal background

Since June 2011 Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC [1] has been directly applicable in EU member states. This regulation lays down uniform criteria and procedures for granting authorisations for placing plant protection products on the market, thereby including rules to ensure the protection of human and animal health and of the environment. Under Article 68 Member States are required to carry out official controls in order to enforce compliance with the regulation. This includes amongst others the topics of production, formulation and parallel trade of plant protection products. For this purpose formulation analysis of plant protection products plays a key role. This analytical work is performed by specialised laboratories designated by the member states. It is of substantial interest that this work is performed in an effective and efficient way, both in terms of the analytical data generated and costs incurred. As of 14 December 2019 Regulation (EU) 2017/625 [2] which contains additional provisions regarding official controls will become applicable.

To date no documents have been developed with regard to useful and efficient approaches for formulation analysis of plant protection products in the area of official control activities. Concerning official controls by EU member states, Article 68 of Regulation 1107/2009 does not state the exact procedure for conducting controls or the scope of analysis that should be performed. For this reason member states have devised their own approaches, resulting in laboratory tests of plant protection products being conducted in different ways and to various extents with regard to analytical methods and techniques. In connection with the non-uniform systems operated in individual member states for taking samples from the market for control purposes, this could result in significant differences in the effectiveness of official controls and makes comparisons of the rates of non-compliant plant protection products between Member States very difficult.

Therefore, this document has been produced as a general guide for laboratories which carry out formulation analysis of plant protection product samples collected during official controls. It lays down analytical strategies, which, upon implementation across EU member states, should increase and harmonise the effectiveness and efficiency of official controls of plant protection products. This guide contains suggested workflows for those cases that laboratories usually encounter in their daily work, i.e. testing samples collected during routine controls (original products, parallel trade products) and testing so-called suspicious samples. However, this guideline does not provide detailed information on analytical methodologies to be used in the course of formulation analysis; laboratories need to obtain such information from relevant publications or carry out own method developments. The introduction of the proposed workflows in the individual laboratories should result in a systematic way of laboratory testing of the quality of plant protection products.

This document describes the best practices used within the EU and commonly accepted criteria for the interpretation of the analytical results generated by the formulation analysis laboratories. The uniform application of these approaches across EU member states should ensure consistent decision making in the evaluation of the analytical results. In this context one has to be aware that a complete analysis of a plant protection product is only possible in rare cases when the composition of the product is very simple. In most cases only certain constituents and/or aspects of the product can be analysed and the decision making has to be performed with the resultant limited information.

This reference document deals with formulation analysis of samples of plant protection products placed on the market as defined under Article 3 (9) of Regulation 1107/2009 in the context of official controls and provides analytical strategies and best practices for the interpretation of analytical results solely in that context. It does not deal with formulation analysis performed in the course of authorisation processes.

It is planned to revise this reference document at regular intervals.

II. Samples for formulation analysis

Wherever possible, the sampling officer should take a complete, unopened plant protection product container as sample. The seal on the container should not be broken until a sub-sample is taken within the analytical laboratory. Where this is not possible, e.g. when sampling intermediate bulk containers, sampling must be carried out in a representative way, the sample transferred to a suitable inert container and immediately shipped to the laboratory.

Upon receipt, laboratories need to assess the integrity of samples and their suitability for analysis. Samples may be considered unsuitable for analysis by the laboratory for a number of reasons, including:

- Sample cannot be identified unambiguously
- Damaged packaging
- Suspicion of tampering with the sample (e.g. broken seal)
- Obvious deterioration of the sample

Where samples are considered unsuitable for analysis, the reason for this decision must be justified and documented.

In general, it is recommended that there remains a period of at least three months before the expiry date of the sample (if such an expiry date exists) when the sample reaches the laboratory. However, analysis may still be performed in other circumstances if requested by the authority. The sample must be stored in the laboratory according the manufacturer's instructions.

As samples may be taken for various specific purposes and under different circumstances, it is useful to differentiate between different sample types and define them, as a suitable approach to formulation analysis may be considerably different depending on the sample type. The workflows for formulation analysis described in the following chapter are tailored towards these different sample types.

Routine samples are either original plant protection products or parallel trade products (for definitions of these terms see below) taken according to a sampling plan. They are analysed to check compliance with the conditions of the authorisation. For these samples there is no prior indication of non-compliance.

Suspicious samples may also be either original products or parallel trade products. They are taken as part of an investigation which is triggered by one of many possible specific scenarios (e.g. observations of inspectors during routine controls, notification of the authority). In any case there exists a certain incident which raised the suspicion that the sample may be non-compliant.

Possible incidents which raise suspicion include, but are not limited to:

- Report of crop damage or non-effectiveness of plant protection product
- Complaint from company or users
- Information from other authority (e.g. customs, financial police)

- Case from another country
- Anonymous tip-off
- Non-compliance of the same plant protection product in a previous control
- Incorrect labelling on plant protection product container or packaging holding product containers
- Incorrect seal or lack of seal on the product container
- Inconsistent or missing documents

Original products are plant protection products that have been authorised according to Article 28 of EU Regulation 1107/2009 [1].

Parallel trade products are plant protection products that are authorised in one EU member state (member state of origin) and have obtained a parallel trade permit in another member state (member state of introduction) on the basis that this plant protection product is identical in composition to a plant protection product already authorised in the member state of introduction (reference product) according to Article 52 of EU Regulation 1107/2009 [1].

Reference samples are samples of original plant protection products which may be obtained for comparison with parallel trade samples or suspicious samples. Reference samples should ideally be obtained directly from the company holding the original authorisation (for parallel trade products: in the member state of origin) but may also be obtained from the market. When using a reference sample the laboratory must ensure that the reference sample complies with the current authorisation. Therefore, a reference sample must be checked for validity, as far as possible/reasonable.

III. Analytical strategies

1. Requirements and general approach

In order to be able to perform formulation analysis of plant protection products taken during market control in an efficient and effective way, laboratories need to be equipped with the necessary equipment and have sufficient staff to competently carry out the respective analyses. Besides standard laboratory equipment and facilities as well as specialised glassware and instrumentation for physical, chemical and technical testing, the laboratories should possess, or at least have access to, chromatographs (HPLC and GC instruments) and mass spectrometers. In particular, a GC-MS instrument is considered to be of utmost importance, whereas LC-MS/MS instrumentation is currently seen as non-essential but may become more useful in the future.

In addition to appropriate equipment, laboratories must also have access to (confidential) information about the analysed plant protection products within a short period of time. From the product labelling, only information on the formulation type and the active substance(s) can be obtained. The laboratories, however, must be provided with the full composition of the plant protection product as submitted during the authorisation process and any subsequent amendments such as the composition of the co-formulants. Additional data submitted during the authorisation process which describe physical, chemical and technical properties can also be useful and should ideally be provided by the respective authority.

The analytical strategies described below have been developed by laboratory experts as standardised best practice models, which provide efficient and effective workflows and which should in general be followed, wherever possible. Obviously, laboratories not being in the possession of certain instrumentation will have to skip certain steps; however, they should still proceed with the general workflows mapped out below. The described workflows should always be critically assessed in the light of each plant protection product sample, as individual cases may suggest an alternative approach. In such cases, however, the laboratory should be able to justify its different approach (e.g. in the course of an audit).

The analytical strategies should be followed step by step, starting with the first one and then working one's way through the succeeding ones. In this way the analyses deemed to be most important/useful and having a higher probability for yielding a non-compliance will be performed first, whereas other methods of lesser importance and with a lower probability of resulting in a non-compliance will follow later. This approach applies especially to laboratories with limited capacities. Alternatively, for laboratories with larger capacities it may be more appropriate to carry out several adjacent steps in parallel. Depending on available resources and analytical possibilities laboratories may decide to quit the workflow at a certain point, however, it is recommended that at least those steps marked with an asterisk in the respective analytical strategy be carried out. In this context, laboratories may also consider the possibility of carrying out certain analyses in a laboratory of another member state. There is a list of formulation analysis laboratories and their scope of analysis located in the Pesticide

Formulation Analysis folder on CircaBC. Of course every laboratory is free to perform additional analyses not mentioned if they judge them be to be useful.

Should a non-compliance be unequivocally determined at any of the steps, the analysis can be considered complete and no further investigations need to be carried out. On the other hand, it must be considered that it is not generally possible to prove full compliance of a sample with the composition as submitted during the authorisation process (although it might be achievable in some cases). However, testing should be conducted as far as reasonably possible. This reasonable extent is laid down in the following analytical strategies.

Prior to analysis the sample must be sufficiently homogenised and any required sub-sampling must be performed in a representative way. These tasks should be carried out according to a written standard operating procedure of the laboratory. Special care needs to be taken for granular samples consisting of granules of different sizes. In these cases it may be necessary to take more than one sub-sample and analyse the sub-samples independently to obtain a true picture of the sample. In the case of a potential non-compliance the suitability of the chosen sub-sampling approach should be assessed critically.

In general the number of replicates performed for each analysis is at the discretion of the laboratory, however, in the case of a potential non-compliance at least a duplicate analysis must be carried out.

2. Differentiation between different analytical strategies according to sample type

The analytical strategy which should be followed depends on the type of sample (see chapter II) and whether a reference sample is used in the course of analysis. The following flow chart depicts the selection path for choosing the appropriate analytical strategy according to the sample at hand.

For suspicious samples it is useful to consider whether the incident that raised the suspicion points towards a certain component or property of the sample (e.g. crop damage by an insecticide may suggest a contamination with a herbicide). Should this be case, this component/property should be assessed as a first step, before proceeding with the general analytical strategy.

In every case the question to be answered by the analysis is: “Is there an unacceptable deviation from the formulation as defined in the conditions of authorisation?”.

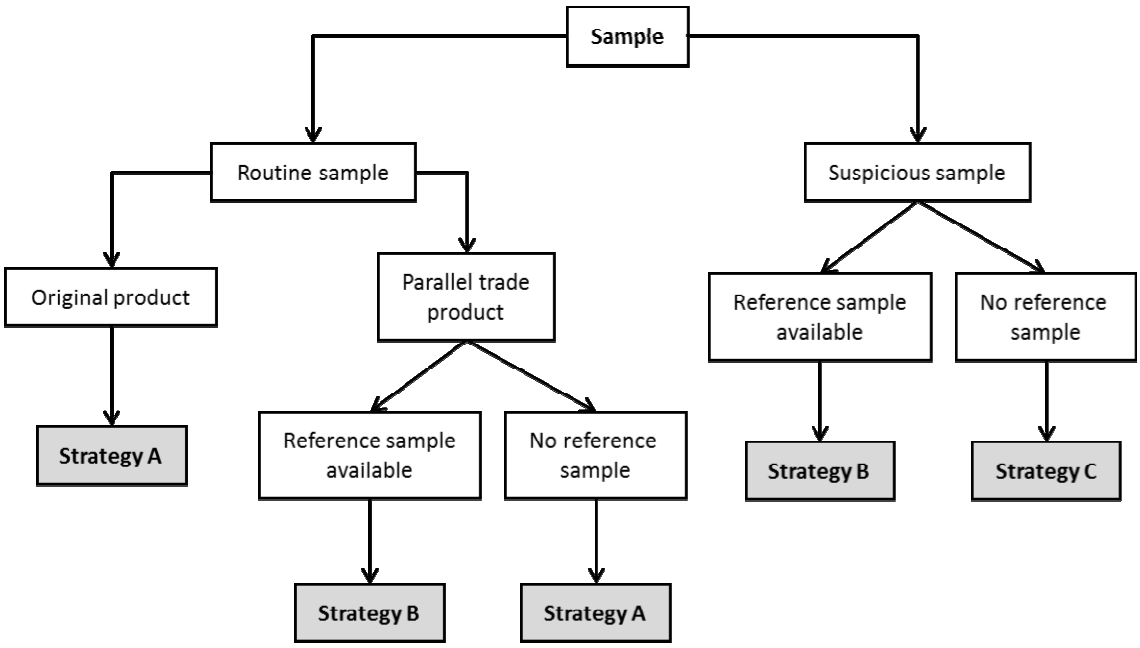

Figure 1. Flow chart for selecting the appropriate analytical strategy

Strategy A

Step 1[*)]: Appearance

Step 2[*)]: Active substance(s) identity and content[1)]

Step 3[*)]: GC-MS screening *or*
physical, chemical and technical properties[2)]

Step 4: Physical, chemical and technical properties[3)]

Step 5: Co-formulants identity[4)] and content

Step 6: Relevant impurities identity[4)] and content[5)]

[*)] steps that are recommended to be carried out as a minimum
[1)] including determination of density for liquid formulations
[2)] choice depending on the composition of the plant protection product (the polarity of the ingredients should be considered). If GC-MS screening is deemed useful for the sample then GC-MS screening should be performed, only otherwise (e.g. in the case of a polar WG formulation) the physical, chemical and technical properties should be assessed in this step.
[3)] if not already performed in step 3
[4)] if not already assessed in step 3
[5)] possibly include in step 2 if there are many samples with the same active substance

Strategy B

Step 1[*)]: Appearance

Step 2[*)]: Profiling by GC-MS, FTIR spectroscopy, GC-FID, LC-UV, LC-MS, NMR spectroscopy or any other suitable technique or a combination of these[1)]

Step 3[*)]: Physical, chemical and technical properties

Step 4[*)]: Active substance identity[2)] and content

Step 5: Co-formulants identity[2)] and content

Step 6: Relevant impurities identity[2)] and content

[*)] steps that are recommended to be carried out as a minimum

[1)] the selection of technique(s) will depend on the instrumentation available in the laboratory and on the composition of the plant protection product (the polarity of the ingredients should be considered). If a significant difference in content of an active substance, relevant impurity or co-formulant is observed at this stage, the quantification of this substance (step 4, 5 or 6) should be carried out before continuing with step 3.

[2)] if not already assessed in step 2

Besides comparing the parallel trade sample / suspicious sample with the reference sample, in the course of this analytical strategy the laboratory should of course also look out for deviations from the authorisation or exceedance of limits set for ingredient contents or physical, chemical and technical properties, which are present for *both* the parallel trade sample / suspicious sample and the reference sample, e.g. a change in a co-formulant or an insufficient suspensibility. In such a case the reference sample is obviously not a valid reference and both plant protection products are non-compliant.

Strategy C

Step 1[*)]: Appearance

Step 2[*)]: GC-MS screening[1)]

Step 3[*)]: Active substance identity[2)] and content[3)]

Step 4[*)]: Physical, chemical and technical properties

Step 5: Co-formulants identity[2)] and content

Step 6: Relevant impurities identity[2)] and content

[*)] steps that are recommended to be carried out as a minimum

[1)] the usefulness of GC-MS screening needs to be considered taking into account the composition of the plant protection product (the polarity of the ingredients should be considered). If GC-MS screening is deemed not useful for the sample (e.g. in the case of a polar WG formulation) then this step should be skipped.

[2)] if not already assessed in step 2

[3)] including determination of density for liquid formulations

3. Description of individual methods and remarks thereon

In the following paragraphs some specific remarks and hints are given regarding the individual methods present in the different analytical strategies.

3.1 Active substance

For the analysis of the active substance methods published by CIPAC [3] or other international organisations, methods submitted by the authorisation holder or in-house validated methods (including "multi active substance methods") may be used. Depending on the set-up of the control plan, laboratories may experience the situation that they have to analyse samples with many different active substances. In this case "multi active substance methods" are especially useful as they allow the analysis of a large variety of active substances with the identical/similar analytical parameter and instrumentation setup, thus considerably saving effort and time. For liquid formulations the density must be determined in the course of the active substance content analysis to enable the calculation of the content in g/l. For this purpose CIPAC MT 3 or OECD test 109 should be used. The value stated for the density during the authorisation process must not be used.

3.2 Appearance

The appearance of a sample comprises its physical state (solid/liquid/gas), its colour and its homogeneity. For tablets the tablet integrity is also assessed.

Physical state, colour and tablet integrity are determined by visual observation. Homogeneity is checked after an appropriate homogenisation procedure has been carried out (if required, twice). Homogeneity may also be assessed by visual observation; however, in some cases more elaborate procedures may be appropriate. For example, the determination of the density or active substance content of different layers (e.g. top/middle/bottom of the container) may be a suitable approach.

3.3 Co-formulants

Concerning the analysis of co-formulants it has to be considered that only well-defined small-molecular species are generally amenable to chemical analysis, especially with regard to quantification. The analysis of oligomeric and polymeric co-formulants will often not be possible (at least with acceptable effort and with the equipment usually available in formulation analysis laboratories). In the latter cases certain physical, chemical and technical tests may provide a much easier mean of assessing these components of the formulation, albeit only indirectly. However, some classes of co-formulants, such as solvents, anti-freezing agents and preservatives, can be analysed by standard chromatographic methods. As only very few internationally validated methods exist in this area, the laboratory will usually have to resort to in-house validated methods. As for active substances, multi-methods which encompass a broad range of compounds are seen to be especially useful and efficient in that respect.

3.4 GC-MS screening

GC-MS screening is a quite laborious, yet very useful analysis, in which all volatile components of the sample are separated using a generic temperature program and full scan mass spectra are acquired throughout the entire separation. Prior to GC-MS analysis the sample is extracted/dissolved with an organic solvent, which may introduce a certain discriminatory element. Thus, the choice of solvent needs to be considered carefully (taking into account the polarity of the ingredients) and it might be advisable to use more than one solvent. The acquired data are then evaluated by comparing the mass spectra of the individual chromatographic peaks (which exceed a certain threshold) against an appropriate mass spectral library (database), yielding (preliminary) information on the identity of the sample's components.

If a foreign substance is found in the course of GC-MS screening it needs to be confirmed and quantified. For this purpose, usually an ad-hoc developed GC method based on the screening method will be used.

3.5 Physical, chemical and technical properties

A wide range of methods to assess physical, chemical and technical properties of plant protection products has been developed over the years, however, only a limited number have been assigned generally applicable criteria for evaluation of compliance [4]. Moreover, many physical, chemical and technical tests are limited to certain formulation types. On the other hand, some physical, chemical and technical tests can be quite useful, as they provide fast and comparatively easy – albeit only indirect – information on certain co-formulants that are (very) difficult to analyse otherwise (e.g. persistent foam may provide information on the presence/absence of an anti-foaming agent). Taking these factors into account a table was developed, listing those methods that should be performed for a certain formulation type. Pourability was excluded as there exist some authorised plant protection products which exceed the generally applicable criterion (this situation not being a problem during application practice). The table is given below.

In the table the order in which the physical, chemical and technical tests for a certain formulation type are recommended to be performed are indicated by ranking numbers. This ranking was developed taking into account the required effort and equipment as well as data on the likelihood to establish a non-compliance by an individual test. Depending on available resources and analytical possibilities laboratories may decide to quit physical, chemical and technical testing at a certain point, however, it is recommended to carry out at least those tests marked with an asterisk in the respective column.

Table 1. Tests for physical, chemical and technical properties that should be performed. Part a) Solid formulation types

		Formulation type [a)]													
	Method	DP	DS	DT	EG	EP	GR	SG	SP	SS	ST	WG [b)]	WP [b)]	WS	WT
Surface properties	Wettability (CIPAC MT 53.3)				4	3			3			5	3	2	
	Persistent foam (CIPAC MT 47.3)				1*)	1*)		1*)	1*)	1*)	1*)	1*)	1*)	1*)	1*)
Particulate, fragmentation and adhesion properties	Dustiness (CIPAC MT 171.1)				3		1*)	3				4			
Dispersion properties	Dispersibility (CIPAC MT 174)											3*)			
	Suspensibility (CIPAC MT 184.1)											2*)	2*)		2*)
	Dispersion stability (CIPAC MT 180)				2*)	2*)									
Solution and dissolution properties	Degree of dissolution and solution stability (CIPAC MT 179.1)							2*)	2*)	2*)	2*)				

Table 1 (continued). Tests for physical, chemical and technical properties that should be performed. Part b) Liquid formulation types

		Formulation type [a)]																	
	Method	CS	DC	EC	ES	EW	FS	GD	LS	ME	OD	OL	SC	SE	SL	UL	ZC	ZE	ZW
Density properties	Density (CIPAC MT 3 / OECD 109) [c)]	1*)	1*)	1*)	1*)	1*)	1*)		1*)	1*)	1*)	1*)	1*)	1*)	1*)	1*)	1*)	1*)	1*)
Surface properties	Persistent foam [d)] (CIPAC MT 47.3)	2*)	2*)	2*)	2*)	2*)	2*)			2*)	2*)		2*)	2*)	2*)		2*)	2*)	2*)
Dispersion properties	Spontaneity of dispersion (CIPAC MT 160)	4											4				4		
	Suspensibility [d)] (CIPAC MT 184.1)	3*)					3						3*)				3*)		
	Dispersion stability (CIPAC MT 180)		3*)								3*)			3*)				3*)	3*)
	Emulsion stability (CIPAC MT 36.3)			3*)	3*)	3*)				3									
Solution and dissolution properties	Dilution stability (CIPAC MT 41.1)								2						3				

[a)] the codes for the different formulation types are explained in [4]

[b)] includes WG-SB and WP-SB, respectively

[c)] only for strategy B, as density will already have been determined in the course of the active substance(s) content in strategies A and C

[d)] applicable only for formulations intended to be diluted with water before use

1, 2, 3…: ranking numbers giving the order in which the physical, chemical and technical methods are recommended to be performed for the respective formulation type

*) indicates methods that should performed as a minimum for the respective formulation type

3.6 Profiling analysis

Profiling analysis may be carried out using GC-MS, FTIR spectroscopy, GC-FID, LC-UV, LC-MS, NMR spectroscopy or any other suitable technique (or a combination of techniques). The selection of technique(s) will depend on the instrumentation available in the laboratory and on the composition of the plant protection product (the polarity of the ingredients should be considered). In the course of a profiling analysis a "fingerprint" of the sample is obtained and compared to the "fingerprint" of a reference sample. The "fingerprint" may either be a total ion chromatogram (GC-MS, LC-MS), an UV chromatogram (LC-UV), a FID chromatogram (GC-FID) or an IR or NMR spectrum (FTIR and NMR spectroscopy). The comparison between the "fingerprints" is performed visually and possibly also by chemometric methods (e.g. correlation coefficient, principal component analysis). It is pointed out that the use of GC-MS for the profiling analysis allows not only a comparison of sample "fingerprints" but components may be (preliminarily) identified and compared with the composition of the plant protection product as submitted during authorisation (see paragraph on GC-MS screening).

3.7 Relevant impurities

The relevant impurities that should be assessed are described in EU legislation [5]. For their analysis methods published by CIPAC or other international organisations, methods submitted by the authorisation holder or in-house validated methods may be used.

IV. Results and reporting

The reporting of the results obtained during formulation analysis and of the methods used must be carried out in such a way that any qualified person can correctly interpret the data and draw valid conclusions. It is essential to maintain uniformity in reporting results of the analysis across different samples, both for chemical analysis (e.g. active substances or co-formulants) and for physical, chemical and technical properties. In general, the test report should fulfil the requirements of the current version of the ISO 17025 standard [6].

The analysed parameter (substance or property) must be assigned a unique name. For active substances, relevant impurities and foreign substances it is possible to mention the chemical names in the report in all cases. For non-relevant impurities or co-formulants, which generally constitute confidential information (unless they are listed in the material safety data sheet), it will depend on national legislation whether it is possible or even mandatory to use chemical names or if codes must be used instead.

Quantitative results should be reported as the arithmetic mean of all multiple analyses performed, where applicable. In some cases, e.g. where multiple results show larger than normal variation, it may be useful to report also the individual values for each analysis. The number of significant digits given should be in accordance with the precision of the analysis. It is common to give as significant digits all certain digits plus the first uncertain digit. When carrying out calculations, intermediate rounding should be avoided. Rounding to significant digits should be done after the final calculation of the result.

For every quantitative analysis the associated expanded measurement uncertainty should be available. The measurement uncertainty is calculated for a specified level of confidence (typically 95%) and constitutes a characteristic of the method. Several approaches exist for deriving the measurement uncertainty (see e.g. [7, 8]). The choice which approach is followed for the estimation of the measurement uncertainty is the responsibility of the laboratory. Whether the measurement uncertainty is reported alongside the analytical result or not, depends on the requirements of the customer and how it is considered in the interpretation of the result (see chapter V and Annex I).

The analytical results for a component of the plant protection product should be reported in the same unit as declared on the label for the active substance (g/kg, g/l or % w/w). The result for a physical, chemical or technical property should be reported in the unit as described by the method used. In all other cases (e.g. impurities, foreign substances) the unit chosen to express the result should be common and reasonable, i.e. large numbers of preceding zeros for values smaller than 1 and large values exceeding 1,000 should be avoided.

Certain physical, chemical and technical tests may be performed at different concentrations (dilutions) of the plant protection product (often relating to application rates). The concentration(s) used for the analysis must be given, as must any other parameters that are of

relevance for interpretation (e.g. temperature at which the analysis was performed, CIPAC standard water used).

V. Interpretation of results

1. Appearance

The sample must be in the physical state (solid, liquid or gas) as stated during authorisation. If this is not the case, the sample is non-compliant.

Striking deviations in colour (e.g. blue instead of red) also constitute a non-compliance, whereas differences in colour shade (e.g. light yellow vs. yellow, turquoise vs. blue) are not sufficient to render a sample non-compliant. However, they may hint towards a non-compliance and require further analyses.

With regards to homogeneity especially liquid plant protection products are at a risk of phase separation, e.g. due to overlong storage or an unsuitable composition. Phase separation can result in the formation of a sediment or of two liquid phases. Sometimes separation is not immediately apparent from the outside but becomes evident because of different densities occurring in the different phases. If the sample is still not homogeneous even after an appropriate homogenisation procedure has been performed twice, the sample is classified as non-homogenisable. In this case it is not appropriate to carry out any further analyses, since it is neither possible to take representative subsamples for analysis nor can it be guaranteed that the product can be applied maintaining a consistent composition. Consequently, the sample is non-compliant.

Concerning tablet integrity, no broken tablets are allowed to be present in at least one package containing multiple tablets.

2. Active substances

For liquid formulations the density that was determined for the actual sample must be used for the calculation of the active substance content in g/l. The density value given during the authorisation process must not be used as there are always small differences between the samples used for the authorisation studies and the actual sample in the laboratory. These deviations can induce small differences in the density value and as a consequence affect the calculated content for the active substance, which may lead to a different interpretation.

The measured value for the density must be compared with the value given in the study submitted during the authorisation process. The deviation must not exceed ± 5%, otherwise the sample is non-compliant (see also section on physical, chemical and technical properties). Differences in density can be due to the use of different solvents, surfactants etc.

Regarding permissible deviations from the declared content of the active substance the values given in the manual on development and use of FAO and WHO specifications for pesticides [4] should be used, which are listed in Table 2. The tolerance refers to the mean analytical

result and takes into account manufacturing, sampling and analytical variations [4]. Thus, if a sample yields a value outside of the limit, it is generally considered non-compliant and measurement uncertainty is not considered separately (MU approach 1). In this approach it must be ensured that the measurement uncertainty does not "consume" more than a certain portion of the tolerance (defined by the laboratory), which may be difficult or impossible to achieve for very high concentrations of active substance. An alternative approach is to check whether the entire uncertainty range of the analytical result is outside of the tolerance (MU approach 2). Only in such a case the sample is then judged as non-compliant. Both approaches are currently used in EU member states and no agreement on a harmonised approach could be reached at present. Additional details concerning the dealing with measurement uncertainty are given in Annex I.

Table 2. Permissible deviations between the declared and actual content of an active substance

Declared content in g/kg or g/l [a)]	**Permissible deviation from the declared content**
up to 25	± 15% for homogeneous formulations (EC, SC, SL, etc. [b)]) ± 25% for heterogeneous formulations (GR, WG, etc. [b)])
more than 25 up to 100	± 10%
more than 100 up to 250	± 6%
more than 250 up to 500	± 5%
more than 500	± 25 g/kg or g/l

[a)] in each range the upper limit is included

[b)] the codes for the different formulation types are explained in [4]

In case of a disputed non-compliance, if a declared content is available in both g/kg and g/l, the analytical result should be calculated in g/kg and this value should be used for the evaluation of compliance.

For mixed solid formulations, which are produced by blending individual fully formulated solid products larger permissible deviations should be used, as solids cannot be mixed to produce the degree of homogeneity achievable with liquid mixtures. For these special cases the limits for the active substance content within each component formulation are expanded by applying a corresponding tolerance to the content of the formulation within the mixture [4], as follows:

Active substance upper/lower limit (A) =
declared content of active substance in component +/- permissible deviation (from Table 3)

Component upper/lower limit (C) =
declared content of component in mixture +/- permissible deviation (from Table 3)

Expanded upper/lower limit for active substance in mixed formulation
E = (A * C) / 1000 g/kg

More details and an example calculation are given in Annex II.

3. Impurities

For relevant impurities maximum limits have been set in Regulation (EU) 540/2011 in relation to the technical active substance. For significant impurities maximum limits can be found in the authorisation documents.

The laboratory needs to calculate the limit for the impurity in the plant protection product as follows: If the maximum limit for an impurity in the technical active substance is ≤ A g/kg and the active substance content in the plant protection product is B g/kg (or g/l) then the maximum limit for the impurity in the plant protection product is ≤ A * B / 1000 g/kg (or g/l). An example calculation is given in Annex II.

For assessing analytical results the measurement uncertainty should be taken into account. A default measurement uncertainty of ± 15% for homogeneous formulations and ± 25% for heterogeneous formulations can be applied, if the laboratory can prove that the individual method used for determining the impurity has a measurement uncertainty that is at or below the proposed default values. Otherwise, the actual measurement uncertainty has to be used. If the determined concentration (mean – uncertainty) of the impurity exceeds the maximum limit in the plant protection product then the sample is non-compliant (MU approach 2).

4. Co-formulants

For liquid formulations the density that was determined for the actual sample must be used for the calculation of the content of a co-formulant in g/l. It is not applicable to calculate the content of the co-formulant with the value given during the authorisation process as there are always small differences between the samples used for the authorisation studies and the actual sample in the laboratory. These deviations can induce small differences in the density value and as a consequence affect the calculated content for the co-formulant, which may lead to a different interpretation.

The manual on development and use of FAO and WHO specifications for pesticides [4] provides no information on permissible deviations from the declared content for co-formulants. A system using the doubled values given in the manual on development and use of FAO and WHO specifications for pesticides [4] for active substances as permissible deviations has been employed by some member states for several years. The reason for this

approach is that due to the manufacturing process the contents of co-formulants may vary more than those of active substances. As for active substances there are two different approaches of dealing with the measurement uncertainty of the analytical result among EU member states. As no agreement on a harmonised approach in terms of permissible deviations and dealing with measurement uncertainty could be reached at present, two possible approaches for the interpretation of results for co-formulants have been set by the EU Working Group on Formulation Analysis.

The first approach for interpretation uses the permissible deviations from the declared content of the co-formulant as given in Table 3 (which are the doubled values given in the manual on development and use of FAO and WHO specifications for pesticides [4] for active substances). In this approach for interpretation the measurement uncertainty is considered to be part of the tolerance and does not need to be considered separately (MU approach 1). Thus, as soon as the tolerance is exceeded the sample is non-compliant. Additional details concerning the dealing with measurement uncertainty are given in Annex I.

Table 3. Permissible deviations between the declared and actual content of a co-formulant for the first approach for interpretation

Declared content in g/kg or g/l [a)]	**Permissible deviation from the declared content**
up to 25	± 30 % for homogeneous formulations (EC, SC, SL, etc. [b)]) ± 50 % for heterogeneous formulations (GR, WG, etc. [b)])
more than 25 up to 100	± 20 %
more than 100 up to 250	± 12 %
more than 250 up to 500	± 10 %
more than 500	± 50 g/kg or g/l

[a)] in each range the upper limit is included

[b)] the codes for the different formulation types are explained in [4]

The second approach for interpretation uses the permissible deviations from the declared content of the co-formulant as given in Table 4 (the values having been fixed by the EU Working Group on Formulation Analysis). In this second approach the entire uncertainty range of the analytical result needs to be outside of the tolerance for a sample to be judged non-compliant (MU approach 2). Additional details concerning the dealing with measurement uncertainty are given in Annex I.

Table 4. Permissible deviations between the declared and actual content of a co-formulant for the second approach for interpretation

Declared content in g/kg or g/l [a)]	Permissible deviation from the declared content
up to 10	± 20 %
more than 10 up to 100	± 10 %
more than 100	± 5 %

[a)] in each range the upper limit is included

Many co-formulants are mixtures of several substances, so called co-formulant substances. When selecting the permissible deviation according to the content in the plant protection product, it is not the content of the co-formulant that has to be considered, but the content of the co-formulant substance. Thus, if the content of the co-formulant is A g/kg (or g/l) and this co-formulant contains a co-formulant substance X at B % then the content of the co-formulant substance X in the plant protection product is C = A * B / 100 g/kg (or g/l) and the concentration C must be used for selecting the permissible deviation from Table 3 or 4, respectively. An example calculation is given in Annex II. If the content of a co-formulant substance is stated as "< x" in the composition of a co-formulant, it only makes sense to check against the upper limit.

If a co-formulant is used as a 'filler' (e.g. water is used as filling agent in many liquid formulations), this fact needs to be taken into account when evaluating the determined concentration.

Stabilisers are co-formulants which are aimed at protecting the formulation from various influences which may cause degradation of components. They include buffer systems, preservatives, antioxidants and active substance-specific stabilisers. Regarding the interpretation of results a difference must be made between degradative stabilisers (e. g. preservatives, antioxidants, biocides) and non-degradative stabilisers (e. g. buffer systems). The concentration of degradative stabilisers can decrease with the age of the sample, whereby the decrease does not necessarily occur continuously. For this reason it is possible that the content of a degradative stabiliser is significantly below its nominal value and it is therefore not appropriate to stipulate a lower limit in these cases.

If the workload required for the quantification of a co-formulant is too high, a qualitative determination will still be useful, since the absence of a declared co-formulant will render the sample non-compliant, under the provision that the LOD of the employed method is significantly below the declared content. It is suggested that the LOD should not exceed 50% of the declared content.

5. Profiling analysis

The obtained "fingerprint" of the sample is compared to the "fingerprint" of a reference sample or library data. The comparison is performed visually and possibly also by chemometric methods (e.g. correlation coefficient, principal component analysis). It has to be considered that small differences between two samples may arise from measurement reproducibility and batch-to-batch variation of sample components. Therefore, a decision if a difference between the sample and its reference sample or the sample and library data is significant and hence renders the sample non-compliant will have to be made by expert judgement and on a case-by-case basis. On the other hand, one has to be aware that small differences between samples may not necessarily show up in the profile comparison, depending on the used technique.

6. GC-MS screening

The (preliminarily) identified compounds detected in the course of GC-MS screening are compared with the composition of the plant protection product as submitted during authorisation, taking into account all available chemical and technological knowledge on the individual compounds (e.g. amenability to GC analysis, relevant and significant impurities of the active substance(s), purity of compounds originating from natural sources, composition of co-formulants, variations between batches of co-formulants composed of mixtures (e.g. Solvesso solvents)). In this way additional, changed or missing compounds can be established. Changed compounds (e.g. different anti-freeze agent: ethylene glycol instead of propylene glycol) constitute a non-compliance. For apparently missing compounds a sufficient sensitivity of the method must be ensured, e.g. by spiking the sample with the compound at its expected level. The possibility of the compound being a degradative stabiliser (cf. section on co-formulants) must be taken into account. If the absence of a (stable) compound is determined with certainty, the sample is non-compliant. Additional compounds, so-called foreign substances need to be confirmed and quantified. Details on this are given in the following section.

7. Foreign substances

When a foreign substance is (preliminarily) identified in the course of GC-MS screening its identity should be confirmed by a reference compound and its concentration needs to be quantified. On the basis that all impurities in a technical active substance above 0.1% need to be declared [9] and other legislation also relating to a 0.1% safety level [10] a maximum level for foreign substances is set at 0.1%. For substances that are very toxic, ecotoxic or phytotoxic, the tolerable amount may be even lower. A limit below 0.1% also applies when the foreign substance is another active substance and its maximum residue limit for harvested produce cannot be complied with.

For assessing analytical results the measurement uncertainty should be taken into account. A default measurement uncertainty of ± 15% for homogeneous formulations and ± 25% for heterogeneous formulations can be applied, if the laboratory can prove that the individual method used for determining the foreign substance has a measurement uncertainty that is at or below the proposed default values. Otherwise, the actual measurement uncertainty has to be used. If the determined concentration (mean – uncertainty) of the foreign substance exceeds the maximum limit in the plant protection product then the sample is non-compliant (MU approach 2).

8. Physical, chemical and technical properties

Regarding the interpretation of results obtained for physical, chemical and technical properties dedicated limits given in a FAO/WHO specification for a certain combination of active substance and formulation type or, if a specification is not present, the general limits stipulated in the manual on development and use of FAO and WHO specifications for pesticides [4] for a certain formulation type should be used. For the physical, chemical and technical properties mentioned in chapter III on analytical strategies (with the exception of density) the general limits of [4] are given in Table 5. If a sample yields a value outside of the limit, it is considered non-compliant. Thereby, the measurement uncertainty is included in the limit and does not have to be considered separately (MU approach 1).

Table 5. Assessment criteria for physical, chemical and technical properties (default limits if no specification is present)

Property, CIPAC method	**Assessment criteria**
Wettability MT 53.3	wetted in 1 min, without swirling
Persistent foam MT 47.3	maximum 60 ml after 1 min, unless there is a warning in the instructions for use
Dustiness MT 171.1	maximum dust of 30 mg (gravimetric method) maximum dust factor of 25 (optical method)
Dispersibility MT 174	minimum 60 %, unless the requirement "only to be used in a tank in which the plant protection product is mixed continuously" is stated
Spontaneity of dispersion MT 160	minimum 60 %, unless the requirement "only to be used in a tank in which the plant protection product is mixed continuously" is stated
Suspensibility MT 184.1	minimum 60 %, unless the requirement "only to be used in a tank in which the plant protection product is mixed continuously" is stated
Dispersion stability MT 180	0 h: initial dispersion complete 24 h: re-dispersion complete
Emulsion stability MT 36.3	0 h: initial emulsification complete 24 h: re-emulsification complete
Degree of dissolution and solution stability MT 179.1	maximum 2 % retained on a 75 µm test sieve
Dilution stability MT 41.1	trace of sediment after 30 min

For density no tolerance is given in [4]. Therefore, an assessment criterion has been fixed by the EU Working Group on Formulation Analysis, which is given in Table 6. If a sample yields a value outside of the limit, it is considered non-compliant. Thereby, the measurement

uncertainty is included in the limit and does not have to be considered separately (MU approach 1).

Table 6. Assessment criterion for density

Property, method	**Assessment criterion**
Density CIPAC MT 3 / OECD 109	± 5% (in comparison to the value given in the study submitted during authorisation)

VI. List of abbreviations

CIPAC	Collaborative International Pesticide Analytical Council
EU	European Union
FAO	Food and Agriculture Organisation
FID	flame ionisation detection
FTIR	Fourier transform infrared
GC	gas chromatography
GC-FID	gas chromatography with flame ionisation detection
GC-MS	gas chromatography coupled to mass spectrometry
HPLC	high-pressure liquid chromatography
IR	infrared
ISO	International Organization for Standardization
LC-MS	liquid chromatography coupled to mass spectrometry
LC-MS/MS	liquid chromatography coupled to tandem mass spectrometry
LC-UV	liquid chromatography with ultraviolet detection
LOD	limit of detection
MS	mass spectrometry
MT	Miscellaneous Techniques [3]
MU	measurement uncertainty
NMR	nuclear magnetic resonance
OECD	Organisation for Economic Co-operation and Development
UV	ultraviolet
WHO	World Health Organisation

VII. Glossary

Co-formulant

Co-formulants are substances or mixtures of substances which provide the plant protection product with certain properties needed for application or stability without having a biological efficacy like active substances.

Co-formulant substance

Co-formulants can consist of several compounds, which are called co-formulant substances. In the authorisation procedure the exact quantities of all co-formulants contained in a plant protection product are stated together with the co-formulant substances they are made up of.

Foreign substance

Foreign substances are compounds, which do not fall into the categories active substances, co-formulants or impurities declared by the authorisation holder. These substances have not been evaluated and are not covered by the authorisation.

Identity

The term identity has several meanings in different circumstances and legislations. In the context of this reference document identity describes the qualitative evidence of a chemical substance.

Impurity

With respect to the technical active substance an impurity is defined in Article 3 (33) of Regulation (EU) No 1107/2009 [1] as “any component other than the pure active substance and/or variant which is present in the technical material (including components originating from the manufacturing process or from degradation during storage)”. Impurities are divided into significant and relevant ones.

In an analogous way an impurity of a co-formulant is defined as any component other than the pure co-formulant substance(s) which is present in the co-formulant.

Must

Must within this document means an absolute requirement; the action is mandatory.

Non-compliance
Non-compliance refers to a breach of a legal limit or a significant, non-acceptable deviation from authorisation conditions. A sample is non-compliant if one of its components or properties is evaluated to be outside of a tolerance range or exceeds a (maximum) limit.

Out of specification
This term is frequently used as a synonym for non-compliance.

Profiling analysis
A profiling analysis is a type of overview analysis where a "fingerprint" of the sample is obtained and compared to "fingerprint" of a reference sample. Typically, profiling analysis is performed by spectroscopy or a separation technique. In profiling analysis it is generally not known which compound is responsible for a certain signal. The compounds of the sample are not identified during profiling analysis. Thus, differences showing up in profiling analysis generally cannot be linked to a certain compound.

Relevant impurity
According to Regulation (EU) No 283/2013 [9] relevant impurities are impurities of the technical active substance that are particularly undesirable because of their toxicological, ecotoxicological or environmental properties. They are specified in the course of authorisation of the active substance and are listed in Regulation 540/2011 [5] together with their maximum limits.

Screening analysis
A screening analysis is a type of overview analysis where all compounds of the sample that are amenable to the employed analytical technique and exhibit a signal exceeding a certain threshold are (preliminarily) identified by a database search. Typically, screening analysis is performed by a combination of a separation technique with full-scan mass spectrometry. The list of (preliminarily) identified compounds is then compared with the composition of the plant protection product as submitted during authorisation.

Should
Should within this documents means a recommendation which may be ignored but only in certain circumstances based on valid reasons. The implications of ignoring the recommendation must be understood and carefully assessed before choosing a different course of action.

Significant impurities

According to Regulation (EU) No 283/2013 [9] significant impurities are all impurities that are present in the technical active substance at concentrations of 1 g/kg or more, with the exception of those compounds being relevant impurities.

VIII. References

EU legal acts and standards quoted refer, where applicable, to the last amended version.

[1] Regulation 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. Official Journal of the European Union, **2009**, L 309, 1-50.

[2] Regulation (EU) 2017/625 of the European Parliament and of the Council of 15 March 2017 on official controls and other official activities performed to ensure the application of food and feed law, rules on animal health and welfare, plant health and plant protection products, amending Regulations (EC) No 999/2001, (EC) No 396/2005, (EC) No 1069/2009, (EC) No 1107/2009, (EU) No 1151/2012, (EU) No 652/2014, (EU) 2016/429 and (EU) 2016/2031 of the European Parliament and of the Council, Council Regulations (EC) No 1/2005 and (EC) No 1099/2009 and Council Directives 98/58/EC, 1999/74/EC, 2007/43/EC, 2008/119/EC and 2008/120/EC, and repealing Regulations (EC) No 854/2004 and (EC) No 882/2004 of the European Parliament and of the Council, Council Directives 89/608/EEC, 89/662/EEC, 90/425/EEC, 91/496/EEC, 96/23/EC, 96/93/EC and 97/78/ EC and Council Decision 92/438/EEC (Official Controls Regulation). Official Journal of the European Union, **2017**, L 95, 1-142.

[3] www.cipac.org

[4] Food and Agriculture Organization of the United Nations and World Health Organization. Manual on development and use of FAO and WHO specifications for pesticides. First edition–third revision. ISBN 978-92-5-109265-1, **2016** (available from www.fao.org).

[5] Commission Implementing Regulation (EU) 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. Official Journal of the European Union, **2011**, L153, 1-186.

[6] ISO/IEC 17025 General requirements for the competence of testing and calibration laboratories.

[7] Eurachem/CITAC guide: Quantifying uncertainty in analytical measurement. Third edition. ISBN 978-0-948926-30-3, **2012** (available from www.eurachem.org).

[8] NT Technical report 53: Handbook for Calculation of Measurement Uncertainty in Environmental Laboratories. Edition 3.1. **2012** (available from www.nordtest.info).

[9] Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products

on the market. Official Journal of the European Union, **2013**, L 93, 1-84.

[10] Maximum concentration levels for foreign substances in plant protection products, http://www.bvl.bund.de/EN/04_PlantProtectionProducts/01_ppp_tasks/08_ProductChemistry/01_ppp_coformulants_formulationChemistry/04_ppp_max_conc_foreign_subst/ppp_max_conc_foreign_subst_node.html (accessed February 11, 2019)

Annex I Measurement uncertainty and assessment of compliance

In order to utilise a result to decide whether it indicates compliance or non-compliance with a limit, it is necessary to take into account the measurement uncertainty. Different approaches may be followed in that respect and it is the responsibility of the laboratory which approach is used.

The first approach (MU approach 1) is to use the definition of the FAO/WHO tolerances [4]. The tolerance given for an active substance refers to the average analytical result and accounts for the variations which usually occur between batches, during sampling and in the analytical determination. The last type of variation may be understood as measurement uncertainty. It should be noted that the variation of the replicate analytical results must lie considerably below the tolerable deviation used as a basis for interpretation. The laboratory should define to what extent the measurement uncertainty is allowed to "consume" the total tolerance and have rules in place for those cases, where the measurement uncertainty "consumes" a higher part of the tolerance than generally allowed. Although not regulated in [4] the same approach may be applied to the judgement of results for co-formulant substances.

The second approach (MU approach 2) considers a result non-compliant, if the measured value is outside the limit by at the least the measurement uncertainty.

Figure 2 shows typical scenarios for a result and its associated measurement uncertainty in relation to the FAO/WHO tolerance ranging from the lower to the upper limit. In the figure the Gaussian curve indicates the probability function for the true value with the apex constituting the measured mean value. Cases (I) and (IV) are clear; the measurement results and their uncertainties provide good evidence that the true value is well outside or inside the tolerance, respectively. In case (II) there is a high probability that the true value is outside of the limit, but the limit is nonetheless within the range of measurement uncertainty. In case (III) the probability that the true value is outside of the limit is small but this possibility cannot be completely disregarded. In MU approach 2 only case (I) would be judged as the result being non-compliant.

In contrast in MU approach 1 both case (I) and case (II) would be judged as the result being non-compliant.

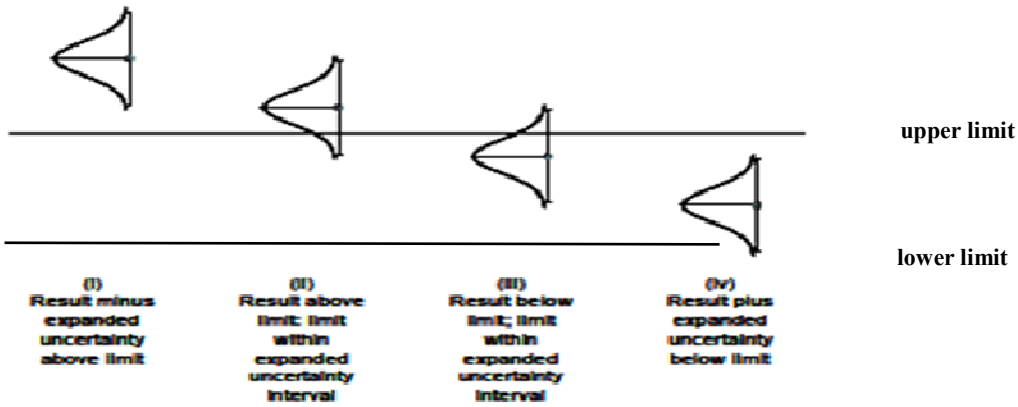

Figure 2. Typical scenarios of the assessment of compliance with the tolerance

Annex II Examples for calculations

1. Expanded permissible deviations for active substances in mixed solid formulations

For mixed solid formulations, which are produced by blending individual fully formulated solid products expanded tolerances as described in Appendix J of the manual on development and use of FAO and WHO specifications for pesticides [4] should be used as permissible deviations for the active substance content. For the calculation of the expanded tolerances it is necessary to know both the contents of the active substances in the original formulations which are blended as well as the contents of the original formulations in the mixed formulation.

The calculation is performed as follows:

(1) Calculate the upper and lower limits for each active substance present in each formulation component of the blend, referring to the permissible deviations given in Table 3:

Active substance upper limit in its formulation (A_u) = g/kg declared + tolerance

Active substance lower limit in its formulation (A_l) = g/kg declared – tolerance

(2) Calculate the upper and lower limits for each component in the blend, applying the permissible deviations intended for the active substance content given in Table 3:

Blend component upper limit (C_u) = g/kg declared + tolerance

Blend component lower limit (C_l) = g/kg declared – tolerance

(3) Calculate the upper and lower limits for each active substance in the blend:

Active substance upper limit in the blend $E_u = (A_u \times C_u) / 1000$ g/kg

Active substance lower limit in the blend $E_l = (A_l \times C_l) / 1000$ g/kg

Example calculation:

Formulation A, declared to contain active substance X at 15% (150 g/kg), is blended with formulation B, declared to contain active substance Y at 50% (500 g/kg). The declared ratio of the formulations A and B in the blend is 70/30 and therefore the declared contents of X and Y in the blend are 10.5% (105 g/kg) and 15% (150 g/kg), respectively.

Active ingredient X:
(1) According to Table 3 the permissible deviation for the active substance X in formulation A is ± 6% (which is equal to ± 9 g/kg) and therefore its upper and lower limits in A are:

$A_u = 150 + 9 = 159$ g/kg

$A_l = 150 – 9 = 141$ g/kg

(2) Applying the permissible deviations intended for the active substance content given in Table 3 to the formulation, the tolerance for formulation A in the blend is ±25 g/kg and therefore its upper and lower limits in the blend are:

$C_u = 700 + 25 = 725$ g/kg

$C_l = 700 – 25 = 675$ g/kg

(3) The upper and lower limits of active substance X in the blend are therefore:

$E_u = (159 \times 725) / 1000 = 115.3$ g/kg

$E_l = (141 \times 675) / 1000 = 95.2$ g/kg

Active ingredient Y:
(1) According to Table 3 the permissible deviation for the active substance Y in formulation B is ± 5% (which is equal to ± 25 g/kg) and therefore its upper and lower limits in B are:

$A_u = 500 + 25 = 525$ g/kg

$A_l = 500 – 25 = 475$ g/kg

(2) Applying the permissible deviations intended for the active substance content given in Table 3 to the formulation, the tolerance for formulation B in the blend is ± 5% (which is equal to ± 15 g/kg) and therefore its upper and lower limits in the blend are:

$C_u = 300 + 15 = 315$ g/kg

$C_l = 300 – 15 = 285$ g/kg

(3) The upper and lower limits of active substance Y in the blend are therefore:

$E_u = (525 \times 315) / 1000 = 165.4$ g/kg

$E_l = (475 \times 285) / 1000 = 135.4$ g/kg

2. Content of an impurity

The plant protection product contains 380.7 g/l technical chlorothalonil (corresponding to 375 g/l pure chlorothalonil). For chlorothalonil hexachlorobenzene was defined as relevant impurity, which must not be higher than 0.04 g/kg in the technical active substance. Based on this information, the maximum limit for hexachlorobenzene in the plant protection product is:

0.04 * 380.7 / 1000 = 0.015228 g/l

3. Permissible deviations for co-formulant substances

A plant protection product contains 110 g/l of a co-formulant A which consists to 50 % of co-formulant substance X. This means that the product contains 55 g/l of co-formulant substance X. When using the first approach for interpretation, according to Table 3 a value of ± 20 % must be considered as permissible deviation for the calculation. The following acceptable range results for co-formulant substance X:

44 g/l – 66 g/l

The measurement uncertainty is considered to be part of the tolerance and does not need to be considered separately (MU approach 1).

When using the second approach for interpretation, according to Table 4 a value of ± 10 % must be considered as permissible deviation for the calculation. The following range results for co-formulant substance X:

49.5 g/l – 60.5 g/l

The entire uncertainty range of the analytical result needs to be outside of this range for a sample to be judged non-compliant (MU approach 2).

If the content of a co-formulant substance is stated as "< x" in the composition of a co-formulant, it only makes sense to calculate an upper limit. For a co-formulant substance with a content < 5 g/l in the plant protection product (homogeneous formulation type) the following applies.

When using the first approach for interpretation, according to Table 3 a value of + 30 % must be considered as permissible deviation for the calculation.

< 5 g/l + 1.5 g/l (corresponding to a maximum value of 6.5 g/l)

The measurement uncertainty is considered to be part of the tolerance and does not need to be considered separately (MU approach 1).

When using the second approach for interpretation, according to Table 4 a value of + 20 % must be considered as permissible deviation for the calculation.

< 5 g/l + 1 g/l (corresponding to a maximum value of 6 g/l)

The entire uncertainty range of the analytical result needs to be above this maximum value for a sample to be judged non-compliant (MU approach 2).