SANTE/2020/12830, Rev.2
14. February 2023

Guidance Document on Pesticide Analytical Methods for Risk Assessment and Post-approval Control and Monitoring Purposes[1]

Supersedes Guidance Documents SANCO/3029/99[2] and SANCO/825/00[3]

Version history

Version	Year	Reasons for update
SANCO/3029/99		
Rev. 4	2000	Original version
SANCO/825/00		
Rev. 6	2000	Original version
Rev. 7	2004	Minor revision
Rev. 8	06/2010	Implementation of changes from Regulation (EC) No. 396/2005 and OECD (ENV/JM/ENV/JM/MONO(2007)
Rev. 8.1	11/2010	Revised version
SANTE/2020/12830 (combined guidance)		
Rev. 1	2021	Implementation of changes from Regulation (EU) No 283/2013 & 284/2013, Harmonisation of validation requirements
Rev. 2	2023	Modification of section “Hazardous reagents”

[1] This document has been conceived as Technical Guidelines of the Commission Services. It does not represent the official position of the Commission. It does not intend to produce legally binding effects. Only the European Court of Justice has jurisdiction to give preliminary rulings concerning the validity and interpretation of acts of the institutions of the EU pursuant to Article 267 of the Treaty.

[2] SANCO/3029/99: Guidance for generating and reporting methods of analysis in support of pre registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414.

[3] SANCO/825/00: Guidance document on pesticide residue analytical methods.

1 Objective and scope

This document provides guidance to applicants, Member States and EFSA on the validation requirements and assessment for quantitative pesticide analytical methods for risk assessment and post-approval control and monitoring purposes (thereafter called “risk assessment methods” and “monitoring methods”) under section 3.5.2 of Annex II of Regulation (EC) No 1107/2009 [1] and of the provisions laid down in sections 4.1.2 and 4.2 of Regulation (EU) No 283/2013 [2], as well as of sections 5.1.2 and 5.2 of Regulation (EU) No 284/2013 [3]. It also applies to applications for setting or modification of a maximum residue level (MRL) within the scope of Regulation (EC) No 396/2005 [4].

This guidance can also be used for active substances approved under the old data requirements according to Regulation (EC) No 544/2011 [5], new MRL applications, MRL reviews, and product authorisations for these substances. Deviations shall be justified with SANTE/11509/2013– rev. 5.2 [6].

It is not intended for biological agents such as bacteria, fungi or viruses.

Risk assessment methods are required to support studies on

- environmental fate
- efficacy
- mammalian toxicology
- operator, worker, resident and bystander exposure
- residues in plants and animal commodities, processed food commodities and feed
- ecotoxicology
- physical and chemical properties

Analytical methods used for determination of physical and chemical properties have been included in this Guidance Document for completeness reasons. However, it has to be noted that the matrix used in these tests is considerably less complex, usually only consisting of water, buffer solution or organic solvent and the substance to be determined. Moreover, the analyte concentration used in the analytical methods for physical and chemical properties is often considerably higher than in the other methods for risk assessment.

Monitoring methods are required to enable Member States to determine compliance with established MRLs in or on food of plant and animal origin, but also for monitoring purposes in soil, water (drinking-, ground- and surface water), air and body fluids and tissues.

For further matrices such as animal feed and fish matrices, there is currently no requirement for monitoring methods, since MRLs have not been set in Regulation (EC) No 396/2005 yet.

In this guidance it is recognised that there will be overlap between requirements for risk assessment and monitoring methods, supporting both. Therefore, requirements have been harmonised where possible.

This guidance document supersedes SANCO/3029/99-rev. 4. and SANCO/825/00-rev. 8.1. It also has been elaborated in consideration of OECD ENV/JM/MONO(2007)17 (Guidance

Document on pesticide residue analytical methods) [7] and SANTE/11312/2021 (Guidance document on analytical quality control and method validation procedures for pesticide residues and analysis in food and feed) [8]. However, it should be noted that the objective of the later guidance document is to give guidance to enforcement laboratories, while this guidance document aims at applicants and risk assessors for approval and authorisation purposes.

It has been conceived as an opinion of the Commission Services and elaborated in co-operation with the Member States. However, it does not intend to produce legally binding effects and by its nature does not prejudice any measure taken by a Member State nor any case law developed with regard to this provision. This document also does not preclude the possibility that the European Court of Justice may give one or another provision of direct effect in Member States.

2 General items

2.1 Good Laboratory Practice

According to Regulation (EU) No 283/2013 and Regulation (EU) No 284/2013, tests and analyses shall be conducted in accordance with the principles laid down in Directive 2004/10/EC [9] where testing is done to obtain data for risk assessment purposes with respect to human or animal health or the environment.

2.2 Description of an analytical method and its validation results

The following information should be offered in the description of the analytical method:

- An introduction, including the scope of the method
- Outline/summary of method, including validated matrices, fortification levels and number of fortifications per level
- Apparatus and reagents
- Description of the analytical method, including extraction, clean-up, derivatisation (if appropriate), chromatographic conditions (if appropriate) and quantification technique
- Sample concentration in the final extract (e.g. g sample per mL extract)
- Instrument parameters used as reference, if appropriate
- Hazards or precautions required
- Time required for one sample set
- Schematic diagram of the analytical method
- Stages where an interruption of the method is possible (if appropriate)
- Result tables (if results are not presented in separate studies)
- Example for the calculation of results from raw data
- Important points and special remarks (e.g. storage conditions, volatility of analyte or its instability with regard to pH, temperature or oxidation)
- References (if needed)

Sometimes it may be necessary to present further information, particularly where special methods are considered.

The submitted studies must include the following validation information:

- Listing of the reference standards, including information on identity (e.g. IUPAC name and molecular mass), purity and expiration date.
- Information (e.g. IUPAC name and molecular mass) on analytes to be quantified, if they differ from the fortified compounds.
- Validation data as described also in sections 3.1 - 3.11
    - Matrix effects
    - Description of calibration procedure, including calibration data
    - Limit of detection (LOD)
    - Limit of quantification (LOQ)
    - Recovery (individual data and mean) and repeatability
    - Data proving the selectivity and specificity of the method
    - Confirmatory data, if required and not presented in a separate study
    - Independent laboratory validation data, if required

- Information on the storage conditions and stability of extracts and standard solutions
- Extraction efficiency of solvents used in methods for food and feed, if not presented in a separate study (see also SANTE 2017/10632 rev. 3 [10]).

2.3 Hazardous reagents

Hazardous reagents classified in accordance with Regulation (EC) No 1272/2008 [11] as carcinogenic (category 1A or 1B), mutagenic (category 1A or 1B) or toxic for reproduction (category 1A or 1B) shall not be used in risk assessment and monitoring methods. Among these compounds are diazomethane, chromium (VI) salts and benzene. In addition, chlorinated solvents, such as chloroform and dichloromethane shall not be used (due to the problematic behavior of chlorinated compounds in the environment and the laborious disposal of waste), except for the purpose of bridging, i.e., comparing solvent extraction of previous methods with new methods. Information on the harmonized classification and labelling of chemical compounds can be consulted on the 'search for chemicals' ECHA website at http://echa.europa.eu/

Methods for risk assessment developed and applied in studies prior to this revision not meeting the above requirement are exempt. However, using such a method in new studies is not acceptable.

2.4 Acceptable analytical techniques considered commonly available

Monitoring methods shall use instrumentation regarded as "commonly available":

Table 1: Analytical techniques considered commonly available for monitoring methods

Chromatography	Detectors	Columns
GC	FPD, NPD, ECD, FID, MS, MS/MS, high resolution MS	Capillary columns, PLOT columns
HPLC/UPLC/IEC	DAD, UV, FLD, MS, MS/MS, high resolution MS	Reversed phase, normal phase including hydrophilic interaction, ion-exchange, porous graphitic carbon
None	AAS, ICP-MS, ICP-OES	-

Other techniques (e.g. chiral columns) can be powerful tools in pesticide analysis; therefore the development of risk assessment methods is not limited to this list.

2.5 Isotopically labelled internal standard (IL-IS)

An isotopically labelled internal standard (IL-IS) differs from the analyte only in terms of the isotopes in the molecule (e.g. deuterium, ^{15}N, ^{13}C, ^{18}O). A prerequisite for the use of IL-ISs is the use of mass spectrometry as detection system and that the stable-isotope labelled standard is largely free of the native analyte so that the quantification is not interfered with. Especially in the case of deuterated standards, it should be noted that an exchange of deuterium with hydrogen atoms can adversely influence quantitative results. IL-ISs may be added at any step of the analytical procedure as appropriate. For example, if added to the final extract prior to analysis, IL-ISs can be used to accurately compensate for matrix effects and response drift in the chromatography-detection system, while if added already prior to extraction, IL-ISs can additionally compensate for both analyte losses and volumetric variations during the procedure. Losses during extract storage (e.g. due to degradation) will

also be corrected for by the IL-IS. Use of IL-ISs will not compensate for incomplete extraction of incurred residues. IL-ISs can be used in risk assessment and monitoring methods.

2.6 Multi-residue methods

Multi-residue methods that cover a large number of analytes and that are based on GC-MS(/MS) and/or HPLC-MS/MS are routinely used in enforcement laboratories for the analysis of plant and animal matrices. Therefore, validated monitoring methods submitted for food of plant and animal origin should be multi-residue methods. Such methods are available from international official standardisation bodies such as the European Committee for Standardisation (CEN) (e.g. [12-15]), the Association of Official Analytical Chemists (AOAC) International (e.g. [16]) or the European Reference Laboratories (EURL) (e.g. [17]). For risk assessment methods, this is not a requirement. If an analyte is not compatible with multi residue methods, or such methods do not exist, a single residue method (see also chapter 2.7) would be acceptable. However, data and/or a justification have to be provided demonstrating that a multi residue method is not applicable.

Examples: An applicant has presented data for a multi-residue method showing unacceptably low recoveries. After modification of the extraction procedure (e.g. by addition of acid or an antioxidant, e.g. ascorbic acid), the recoveries are within an acceptable range. In addition, a typical example of an analyte not being compatible with multi residue methods is the analysis of gaseous pesticides or metabolites included in the residue definition (e.g. phosphane, sulfuryl fluoride, dazomet, metam) requiring headspace analysis.

2.7 Single residue methods and common moiety methods

Risk assessment methods

For risk assessment methods, single residue methods are generally acceptable.

In cases where it is likely that a multi-component residue definition will be required for risk assessment purposes in plants and animals, a common moiety method may be used. However, the choice of appropriate methods should take into consideration the needs of both, risk assessment and monitoring. Where possible, applicants should either:

(i) separately analyse for the individual components of the residue, rather than carrying out a total residue analysis; or

(ii) carry out a total residue analysis of field trial samples to cover the residue definition for risk assessment using a common moiety method, and a second series of analyses using the same samples to cover the marker compounds of the residue definition for monitoring.

Example: The residue definition for risk assessment comprises the sum of compound A + B + C + D + E, and for monitoring compound A. To cover both residue definitions, an applicant could develop according to (I) one method covering all five individual compounds separately. Alternatively, according to (II), the applicant could also develop one common moiety method to cover the residue definition for risk assessment, but then has to develop a second method covering the residue definition for monitoring.

Monitoring methods

For monitoring, single residue methods should only be provided if data show that multi-residue methods cannot be used. The method(s) should be suitable for the determination of all compounds included in the residue definition. If this is not possible and an excessive number of methods for individual compounds would be needed, a common moiety method may be acceptable, provided that it is in compliance with the residue definition.

2.8 Derivatisation

For the GC analysis of some compounds, such as those of high polarity or with poor chromatographic properties, or for the detection of some compounds in HPLC, derivatisation may be required. These derivatives may be prepared prior to chromatographic analysis or as part of the chromatographic procedure, either pre- or post-column. Where a derivatisation method is used, this must be justified and the detailed reactions to obtain the derivatised species should be provided.

If the derivatisation is not part of the chromatographic procedure, the derivative must be sufficiently stable and should be formed with high reproducibility and without influence of matrix components on yield. The efficiency (mean yield) and precision of the derivatisation step shall be demonstrated with analyte in sample matrix against pure derivative. If no pure derivative is available, a justification of the suitability of the derivatisation reaction shall be provided (e.g. by suitable literature data). The storage stability of the derivative should be checked and reported. For details concerning calibration refer to Section 3.2.

The analytical method is considered to remain specific to the analyte of interest if the derivatised species is specific to that analyte. However, where – in case of pre-column derivatisation – the derivative formed is a common derivative of two or more active substances or their metabolites or is an active substance itself, the method is considered non-specific and therefore unacceptable as a monitoring method.

2.9 Hydrolysis

A hydrolysis step may be required if esters, amides and/or conjugates are included in the residue definition and the structures of the conjugates are unknown or no conjugate standard is available. In order to demonstrate the efficiency of the hydrolysis the following approaches can be applied:

- If standards of esters, amides and conjugates are available, they can be determined directly or the efficiency of the hydrolysis can be verified with these standards for each relevant matrix group.
- If no standards are available, but identical conditions are applied as in the metabolism studies, total hydrolysis is assumed if in the metabolism studies the efficiency of the hydrolysis step has been demonstrated and sufficient characterisation/identification has been carried out.
- If no standards are available and hydrolytic conditions differ from those in the metabolism studies, the applicant should verify these conditions by performing a cross-validation study. This could be done using incurred residues from field trials or metabolism studies and comparing the hydrolytic conditions of the method to varying conditions (e.g. use of strong acid or base, refluxing overnight, use of enzymes). The hydrolytic conditions of the method can be considered sufficient, if no additional

conjugates/esters are cleaved by the extreme conditions (±20% are considered acceptable).

2.10 Methods for isomeric mixtures

For pesticides consisting of two or more isomers, the quantification can be performed either as the sum of peak area or height of all isomers or the peak area or height of individual isomers. Enantioselective methods are only required if a single enantiomer is included in the residue definition e.g. to investigate the isomeric behavior of an active substance for risk assessment purposes. For the chromatographic separation of enantiomers, chiral HPLC or GC columns or a chiral modifier of the HPLC eluent is required. In this case, quantification should be performed for the individual enantiomers, provided that sufficient chromatographic resolution can be achieved and reference compounds for individual enantiomers are available.

3 Method validation parameters

Validation data must be submitted for methods for risk assessment and monitoring for all analytes included in the residue definitions and for all representative sample matrices to be analysed at relevant concentration levels.

Basic validation data are:

- Calibration data
- Concentration of analyte(s) found in blank samples
- Concentration level(s) of fortification experiments
- Concentration and recovery of analyte(s) found in fortified samples
- Number of fortification experiments for each matrix/level combination
- Individual recovery data and mean recovery for each matrix/level combination
- Relative standard deviation (RSD) of recovery, separately for each matrix/level combination
- Limit of detection (LOD), corresponding to the lowest calibration standard
- Limit of quantification (LOQ), corresponding to the lowest validated level
- Representative, clearly labelled chromatograms of at least blank samples, lowest calibration standard and fortified samples at lowest fortification level
- Data on matrix effects, e.g. on the response of the analyte in matrix compared to the analyte in solvent
- Data on the stability of extracts and standard solutions

3.1 Matrix effects

Assessment of matrix effects should be performed by comparing the analyte response of at least one individual standard prepared in solvent to at least one prepared in blank matrix, for all sample materials included in the corresponding validation study. Alternatively, the slope of the calibration function prepared with standards in pure solvent can be compared with that for the calibration with standards in matrix. Matrix effects, expressed in % enhancement or suppression can be evaluated according to the following equation:

*Matrix effects [%] = 100 * peak area or slope (matrix)/ peak area or slope (solvent) – 100*

Matrix effects are considered significant if they exceed ±20%.

3.2 Calibration

The analytical calibration must cover at least the range which is suitable for the determination of the fortification levels required and should range from 30% of the LOQ to 20% above the highest fortification level (if necessary after dilution) (Section 3.5).

For monitoring methods, the analytical calibration should cover a maximum of two orders of magnitude. For other types of methods, such as for risk assessment, where the analytical calibration may need to cover more than two orders of magnitude, samples can be diluted to fit within the calibrated range. Alternatively, two calibration curves can be generated (e.g. 1st curve: 0.005 - 0.5 mg/kg; 2nd curve: 0.5 - 5 mg/kg).

If the working range has to cover one order of magnitude, three concentration levels are necessary (each in duplicate determination), while five concentration levels (in single determination) are necessary to cover two orders of magnitude. Standard concentrations should be distributed evenly over the full calibration range.

In order to compensate for matrix effects, calibration can be generated using standards prepared in blank matrix extracts (matrix-matched standards). Other calibration procedures to compensate matrix effects are using IL-IS, standard addition or procedural calibration. However, matrix matched calibration is preferred. Only if experiments clearly demonstrate that matrix effects are not significant (≤±20%), calibration with standards in solvent may be used.

Individual calibration raw data shall be presented at least for each analyte and matrix group (for mass spectrometric detection also each ion/mass transition) together with the equation of the calibration line and the respective calibration plot. Concentration data shall be reported as both, the mass fraction in the original sample (e.g. mg/kg) and the concentration in the final solution (e.g. µg/L).

Calibration should be assessed under consideration of CEN/TS 17061:2020-01 [18]. Linear weighted calibrations (e.g. 1/x weighting) are preferred if shown to be acceptable over an appropriate concentration range. Other continuous, monotonically increasing functions (e.g. exponential/power, logarithmic) may be applied where this can be fully justified based on the detection system used.

The suitability of the chosen function should be demonstrated. Preferably, this should be accomplished by a residual analysis using the residuals, rather than reporting the coefficient of correlation (r) or determination (R^2). The regression residual d_i describes the vertical distance of measured values from the regression curve according to:

$$d_i = y_i - y_{yi}$$

where

y_i is the measured value i;

y_{yi} is the estimated value which corresponds to y_i and is derived from the calibration function.

The regression residuals should be presented in a residual plot. Visual inspection should be applied to decide if d_i are randomly distributed and hence linear calibration is demonstrated. If a trend is visible in the residuals, the calibration model is not suitable and an alternative approach must be used (e.g. alternative calibration function, different/split calibration range).

When quantification is based on the derivatised analyte, the calibration shall be conducted using standard solutions of the pure derivative generated by weighting, unless the derivatisation step is an integral part of the pre- or post-column method. If the derivative is not available as a reference standard, it should be generated within the analytical set by using the same derivatisation procedure as that applied for the samples and full justification should be given.

3.3 Limit of detection

The limit of detection (LOD) is defined as the lowest detectable concentration or amount of an analyte in a sample. It should be expressed as lowest calibration standard, preferably in matrix rather than the value calculated from signal to noise ratio in control samples. The LOD can provide valuable information for risk assessment methods (e.g. methods used in field trials were the LOD could be used for the refinement of the dietary or cumulative risk assessment).

3.4 Limit of quantification

The limit of quantification is defined as the lowest validated level with sufficient recovery and precision (see also 3.5).

- For monitoring methods, the validated LOQ of residue analytical methods should generally be at the default MRL of 0.01 mg/kg for plant and animal commodities. Exceptions are higher default MRLs for difficult matrices such as herbal infusions, spices, hops or lower MRLs for compounds with a very low toxicological reference value. For environmental matrices the LOQ for monitoring methods should be at or below the respective limit values which are derived from eco-toxicological endpoints. In the case of a complex residue definition containing more than one analyte, the method LOQ should be the sum of the individually validated component LOQs (calculated as stated in the residue definition). The combined LOQ must be in agreement with the MRL/limit value.

  Example: The residue definition for monitoring of the active substance A is A + M1 + M2, expressed as A. The lowest MRLs are set at 0.03 mg/kg. Hence, validation should be performed at 0.01 mg/kg for each component, expressed as parent equivalents.

  For further details it is referred to SANCO/12574/2014 [19].

- For analytical methods for risk assessment, the LOQ of residue methods (e.g. in field trials) should be as low as required to meet the study needs, while for dose verification studies (e.g. (eco-)toxicological studies), the LOQ should be at or below the lowest dose.

If chiral analytes are included in the residue definition(s), the LOQ usually applies to the racemate. In this case it is not necessary to determine the enantiomers separately.

3.5 Recovery and repeatability

Recovery and repeatability (as precision, % RSD) data must be reported for the following fortification levels:

- LOQ 5 samples
- 10 times LOQ, or MRL (set or proposed) or other relevant level
  5 samples

It should be noted that the evaluation of repeatability can be performed with samples prepared and analysed in one day or over several days.

Additionally, for unfortified samples, that have undergone the same sample preparation process as the fortified samples, residue levels must be reported as follows:

- blank matrix 2 samples

In cases of complex residue definitions containing more than one compound, the validation results shall be reported for the single components unless they cannot be analysed separately.

For food/feed of plant and animal origin, the acceptable range of mean recoveries and the required precision are specified in Table 2. For all other matrices, the range of mean recoveries at the relevant concentration level should be 70 - 120% and the precision ≤20% RSD.

Table 2: Requirements for mean recovery and precision for food/feed of plant and animal origin

Concentration level (mg/kg)	**Range of mean recoveries (%)**	**Precision, RSD (%)**
≤ 0.01	60 - 120	30
> 0.01 - ≤ 0.1	70 - 120	20
> 0.1 - ≤ 1.0	70 - 110	15
> 1	70 - 110	10

If blank values are unavoidable due to natural background levels or environmental contaminations, recoveries should be corrected and reported along with the uncorrected recoveries (e.g. for copper or dithiocarbamates).

When outliers have been identified using appropriate statistical methods (e.g. Grubbs or Dixons test), they may be excluded from the statistical calculation of mean, SD and RSD, with justification and with the statistical significance, but all individual recovery data (including the excluded ones) shall be reported. The number of outliers must not exceed 1/5 of the results at each fortification level.

3.6 Selectivity and specificity

Representative, clearly labelled chromatograms of standard(s) at the lowest calibrated level, matrix blanks and samples fortified at the lowest fortification level for each analyte/matrix combination must be provided to prove selectivity of the method. Labelling should include sample description, chromatographic scale and identification of all relevant components in the chromatogram. This is not necessary for the determination of specific elements (e.g. copper) analysis using AAS, ICP-OES or ICP-MS (however, absence of interference and matrix effects shall be demonstrated [20]).

When mass spectrometry is used for detection, a mass spectrum (in case of MS/MS: product ion spectrum) should be provided to justify the selection of ions used for determination. For all analytical techniques, blank values (non-fortified samples) must be determined from the matrices used in fortification experiments and should not be higher than 30% of the LOQ. Otherwise detailed justification has to be provided.

3.7 Confirmation

Confirmatory methods are required to demonstrate the selectivity of the primary method for all representative sample matrices. It has to be confirmed that the primary method detects the correct analyte (analyte identity) and that the analyte signal of the primary method is quantitatively correct and not affected by any other compound. No confirmatory method is required for the determination of elements such as copper by AAS, ICP-OES or ICP-MS since the analysis is specific.

3.7.1 Confirmation simultaneously to primary detection

For methods using one fragment ion in GC-MS and HPLC-MS or one transition in GC-MS/MS and HPLC-MS/MS, simultaneous confirmation can be achieved by one of the following approaches:

- In GC-MS, HPLC-MS: by monitoring at least 2 additional fragment ions (preferably m/z >100)
- In GC-MS/MS, HPLC-MS/MS: by monitoring at least 1 additional SRM transition
- High resolution MS: by monitoring 2 ions with a mass accuracy of ≤5 ppm (<1 mDa for m/z <200), preferably including the molecular ion, (de)protonated molecule or adduct ion and at least one fragment ion.

If a confirmatory method is required and performed simultaneously to the primary detection, the following validation data need to be provided for the additional fragment ions (MS and HRMS) or the additional SRM transition (MS^n and MS/MS): calibration data (Section 3.2), recovery and precision data (Section 3.5) for samples fortified at the respective LOQ (n = 5) and for 2 blank samples and proof of selectivity/specificity (Section 3.6).

For all mass spectrometric techniques a mass spectrum (in case of single MS) or a product ion spectrum (in case of MS^n) should be provided to justify the selection of the additional ions.

3.7.2 Confirmation by an independent analytical technique

Confirmation can also be achieved by an independent analytical detection or chromatographic technique. The following confirmatory techniques are considered sufficiently independent:

- Chromatographic principle different from the original method (e.g. HPLC instead of GC)
- Different stationary phase and/or mobile phase with significantly different selectivity
    - The following examples are not considered significantly different:
        - in GC: 100% dimethylsiloxane versus 95% dimethylsiloxane + 5% phenylpolysiloxane
        - in HPLC: C18- versus C8-phases
- Alternative detector (e.g. GC-MS versus GC-ECD, HPLC-MS versus HPLC-UV/DAD)
- High resolution/accurate mass MS
- In mass spectrometry an ionisation technique that leads to primary ions with different m/z ratio than the primary technique (e.g. ESI negative ions vs. positive ions).

It is preferred that confirmation data are generated with the same samples and extracts used for validation of the primary method.

If a confirmatory method is required and uses an independent analytical technique, the following validation data need to be provided: calibration data (Section 3.2), recovery and precision data (Section 3.5) for samples fortified at the respective LOQ (n ≥ 3) and for a blank sample and proof of selectivity/specificity (Section 3.6).

3.8 Independent laboratory validation (ILV)

A validation of the primary monitoring method in an independent laboratory (ILV) is required for the determination of residues in food of plant and animal origin and in drinking water. The ILV shall confirm the LOQ of the primary method, or at least cover the lowest MRL.

In order to ensure independence, the laboratory chosen to conduct the ILV study must not have been involved in the method development. The laboratory may be part of the same company, but should not be in the same location. In case of multi-residue methods, it is acceptable if the ILV is performed in a laboratory that has already experience with the respective method.

The extent of the ILV with regard to the number of samples, fortification levels, recovery and selectivity/specificity must cover the requirements laid out in Section 3.5 – 3.6.

Generally, the ILV should be as close to the original method as possible. However, if in individual cases any additions or modifications to the original method are required, they must be reported and justified. If the chosen laboratory requires communication with the developers of the method to carry out the ILV, this should be reported.

The following table gives an overview of modifications to the primary method and their consequences with regard to the acceptability of the ILV.

Table 3: Examples for acceptable and non-acceptable deviations of the ILV from the primary method

Deviation of ILV from primary method	ILV acceptable	ILV not acceptable
LOQ higher than that of the primary method and > MRL[1]		X

Deviation of ILV from primary method	ILV acceptable	ILV not acceptable
LOQ higher than that of the primary method and < MRL[1]	X (higher LOQ is then considered for the overall method)	
Validation with different crops from same matrix group (e.g. cereal grain <-> dry legumes)	X	
Validation for high water content matrix is missing but ILV for 2 matrices available and primary method identical for all matrices		X
Number of replicates or levels not sufficient		X
Different extraction solvents		X
Additional clean-up steps are performed		X
Use of different laboratory equipment (shaker, vessels, pipets…)	X	
Use of different GC or LC column	X (if justified)	
Use of different mass or transition	X (if justified)	
Use of different calibration models • matrix matched-solvent • linear-quadratic	X (if justified)	
Use of different ionisation mode (ESI+ <-> ESI-)	X (if justified)	
Use of different detection technique (e.g. HPLC-MS<-> HPLC-MS/MS or HPLC-MS/MS <-> HRMS)	X (if justified)	
Modular multi-methods (DFG S19, modular QuEChERS): use of different modules		X

[1] Lowest MRL of commodity from the respective matrix group

3.9 Extract and standard stability

3.9.1 Final extract stability

In order to prevent degradation, final extracts should be stored in a fridge or freezer. In final extracts (without use of IL-IS) not analysed within 24 h, the stability of the analyte is sufficiently proven, if the recoveries in the fortified samples are within the acceptable range of 70 - 120%, measured against freshly prepared standards. If the extracts contain an IL-IS for quantification, testing of final extract stability is not required since the IL-IS will compensate for losses during extract storage.

3.9.2 Standard stability

In order to prevent degradation, standard solutions (stock, calibration etc.) should be stored in a fridge or freezer. Stability of an existing standard should be checked by preparing a new stock standard and comparing the detector responses. The means from at least 5 replicate measurements for each of the two solutions should not differ by more than 10%. Internal standards may be used to reduce measurement variation. More detailed information can be found in SANTE/11312/2021, chapter F [8].

3.10 Extraction efficiency

The extraction procedures used in the methods for risk assessment and post-approval control and monitoring purposes for the determination of residues in food/feed of plant and animal origin should be verified. More details are given in SANTE 2017/10632 rev. 3 [10].

3.11 Availability of standards

All analytical standard materials used in an analytical method for monitoring must be commercially available prior to approval of the active substance at EU level and MRL setting. This applies to metabolites or conjugates being part of the residue definition, derivatives (if preparation of derivatives is not a part of the method description), stable isotope labelled compounds or other internal standards.

4 Validation requirements for quantitative methods for risk assessment

4.1 Validation requirements for methods for risk assessment

Each laboratory involved in the generation of risk assessment data needs to perform its own method validation according to Table 5.

4.1.1 Purpose

Methods for risk assessment are developed for the generation of data in support of environmental fate, efficacy, toxicology, residues, ecotoxicology and physical and chemical properties studies in the context of dossier preparation for regulatory purposes. According to Commission Regulation (EU) No 283/2013, only methods using non-radiolabelled compounds have to be provided for the sections in the dossier listed in Table 4.

Table 4: Examples of studies requiring methods for risk assessment

Dossier section	**Study examples**
Methods for soil, water, sediment, air and any additional matrices used in support of environmental fate studies	• Soil/aqueous degradation studies • Soil dissipation studies • Photolysis studies
Methods for soil, water and any additional matrices used in support of efficacy studies	• Carry over of phytotoxic levels of the a.s. and/or metabolites in soil • Assessing effectiveness of procedures for cleaning spray equipment
Methods for feed, body fluids and tissues, air and any additional matrices used in support of toxicology studies	• Dose verification and homogeneity of test diets and dose preparations • Residue levels in tissues and body fluids • Concentration of test compound in air for inhalation studies
Methods for body fluids, air and any additional matrices used in support of operator, worker, resident and bystander exposure studies	• Residue levels on gloves, wipes, air sampling filters etc. • Dislodgeable residue studies
Methods for plants, plant products, processed commodities, food of plant and animal origin, feed and any additional matrices used in support of residues studies	• Residues in field trials for primary crops • Storage stability studies • Processing studies • Residues in field rotational crop studies • Residues in livestock feeding studies (poultry, ruminant) • Fish feeding studies • Residues in honey
Methods for soil, water, sediment, feed and any additional matrices used in support of ecotoxicology studies	• Dose verification in test water or test soils • Studies on the homogeneity of test diets • Honey bee studies
Methods for water, buffer solutions, organic solvents and any additional matrices used in the physical and chemical properties tests	• Solubility in water and organic solvents • Determination of the octanol/water partitioning coefficient

4.1.2 Selection of analytes

As long as no decision on the residue definition for risk assessment has been set, it is recommended to analyse, besides parent, also metabolites that are potential candidates for being included in the residue definition. On the other hand, if a residue definition for risk assessment has been set, the selection of analytes to be validated can be limited to those compounds included.

4.1.3 Samples

The validation data set can be composed of the respective number of concurrent (procedural) recoveries from matrices of the same matrix group within the same study report. However, just referring to a method validated in a different laboratory is not sufficient.

Example: A laboratory wants to analyse active substance A in rape seeds from field trials for the first time. A total of 5 fortifications at LOQ and 5 at higher levels are interspersed within the sequence as concurrent recoveries. If recovery and repeatability is within acceptable limits, the method can be considered as sufficiently validated for high oil content matrices.

Food/feed of plant origin (raw and processed): Method validation data according to Table 5 must be submitted for the matrix groups covering the commodities of the intended uses. The matrix groups are:

- dry commodities (high protein/high starch content)
- commodities with high water content
- commodities with high oil content
- commodities with high acid content
- matrices difficult to analyse
- dry, high sugar content commodities (processed commodities only, e.g. dried fruits)

An assignment of the commodities to their respective matrix groups is presented in Appendix 1, Table A1 and A2.

Additional commodities belonging to the same matrix group do not require a separate validation. However, the applicability of the method to a different commodity should be demonstrated by concurrent recoveries (minimum 3 recoveries at LOQ and 3 recoveries at a higher level).

For storage stability studies, the group of dry matrices is splitted into high protein content and high starch content matrices. However, since their properties during sample preparation are similar, both matrices are combined here into one matrix group for analytical purposes.

Example: Laboratory A wants to analyse rape forage (high water content) and rape seeds (high oil content) from field trials. According to Table 5, the method has to be validated for one representative commodity with high oil content and one with high water content. Subsequently, laboratory A wants to analyse sunflower seeds (high oil content) from field trials. No additional validation of the method is required since sunflower seeds belong to the same matrix group as rape seeds. Nevertheless, the suitability of the method for sunflower seeds

should be demonstrated with concurrent recoveries. In contrast to that, laboratory B, which also wants to analyse sunflower seeds, but has no prior experience with the method, needs to perform a full validation according to Table 5 for high oil content matrices.

For processing studies, an assignment of the raw agricultural commodity (RAC) and the processed commodities to their respective matrix groups is presented in Appendix 1, Table A3. It should be noted that for dried fruits an additional matrix group (dry, high sugar content) is introduced. Usually, validation of the RAC should be done with a representative commodity of its assigned matrix group. For processed commodities assigned to a matrix group, a validation is only required, if this group has not been covered by the RAC. Nevertheless, the suitability of the method for each processed commodity should be demonstrated with concurrent recoveries (minimum 3 recoveries at LOQ and 3 recoveries at higher level). For processed "difficult" commodities a validation according to Table 5 is always required.

Example: A laboratory wants to perform a study processing citrus fruits into juice, canned fruit, marmalade and citrus oil. A validation of the method according to Table 5 is required for one representative commodity with high acid content to cover the RAC, fruit juice, wet pomace and canned fruit. For citrus oil a separate validation for high oil content matrices is required since citrus oil is not covered by the matrix group of the RAC. Similar, for marmalade a separate validation is required, as it belongs to the commodities with high water content.

Food of animal origin, livestock tissues (poultry, lactating ruminants, pigs and fish): Method validation data must be submitted for the following animal tissues, where appropriate:

- Milk
- Liver or kidney
- Muscle
- Fat
- Eggs
- Muscle/skin (fillet of fish)
- Carcass (fish only)

Honey, pollen and other bee products: As the compositions of royal jelly (composed of water, lipids, proteins and products with an acidic pH) and pollen (composed of proteins, sugars and pigments) are different from the composition of honey, the analytical methods should be validated separately for each matrix. For nectar, a validation in diluted honey is acceptable. For further information please refer to SANTE/11956/2016 rev. 9 [21]

Soil and sediment: Where appropriate, method validation data must be submitted using standard soils or any other appropriate test soils used in environmental fate and/or ecotoxicological studies.

Water: Where appropriate, method validation data must be submitted using water samples according to Section 5.4.3, or any other test water or media used in environmental fate and/or ecotoxicological studies. Extrapolation between different water/media types can be accepted, if they only differ in their composition of salts. In case HPLC-MS/MS is used, the direct injection

of water samples is desirable, provided this complies with the LOQ. While recovery data cannot be calculated in this case, calibration and precision data have to be presented.

Air: Where appropriate, method validation data must be submitted for air according to Section 5.5.3 and 5.5.6 or to cover conditions comparable to those studies where the methodology is used. The detailed sampling conditions (temperature, relative humidity, active or passive sampling, sampling time, air flow, sample material) used should be provided in full.

Body fluids and tissues: Where appropriate, method validation data must be submitted using samples according to Section 5.6.3.

Dislodgeable and transferable residues as well as additional matrices used in support of operator, worker, resident and bystander exposure studies:
Information on dislodgeable and transferable residues is used for an estimation of dermal exposure of workers, residents and bystanders, who have contact with treated plants/turf. For sampling and determination of dislodgeable foliar residues and turf transferable residues, the methods by Iwata et al. [22] and Fuller et al. [23] apply, respectively. Methods for dislodgeable and transferable residues as well as for additional matrices used in support of operator, worker, resident and bystander exposure studies should be fully described and validated as detailed in OECD guidelines [24].

Feed: Where appropriate, method validation data must be submitted for animal test diets or dosing solutions used in (eco)-toxicological and livestock residue studies.

Buffer solutions, solvents etc.: Where appropriate, validation data must be submitted for the determination of the active substance or metabolites in aqueous solutions and in organic solvents.

4.1.4 Validation requirements

The following general validation requirements apply for non-isotope labelled methods for risk assessment developed for the areas mentioned in Table 4, with the exception of methods for physical and chemical properties:

Table 5: Validation requirements for methods for risk assessment

Parameter	Requirement
Matrix effects (according to section 3.1)	Yes
Linearity (according to section 3.2)	Yes
Limit of quantification (according to section 3.4)	Yes
Recovery and repeatability (according to section 3.5)	Yes
Selectivity/specificity (according to section 3.6)	Yes
Confirmation (according to section 3.7)	No
Independent Laboratory Validation (according to section 3.8)	No
Stability of standards and extracts (according to section 3.9)	Yes[1, 2]
Extraction efficiency (according to section 3.10)	Yes[1]

[1] not required if demonstrated in a separate study

[2] not required in the case for extracts if IL-IS is used

4.1.5 Validation requirements for analytical methods in physical and chemical properties determination

Methods for the determination of physical and chemical properties are described in Regulation (EC) No. 440/2008 [25], OECD Test Guidelines or in CIPAC methods. Some of these methods contain validation requirements for the analytical method to be used in the respective test. For examples of studies requiring validated analytical methods for the determination of physical and chemical properties, see Table 4.

In order to judge whether the used analytical method is fit for purpose for the respective physical or chemical property, the following information and data should be generally provided:

- Description of the analytical method and/or referral to a respective standard method if available
- Demonstration of linearity (calibration plot or raw data) where appropriate, e.g. for chromatographic or photometric methods
  The sample concentration must be within the linear range of the calibration.
- Representative chromatograms if LC or GC methods are used

The determination of the specificity, recovery and repeatability of the analytical method is not generally required. This is due to the fact that the analytes are usually pure substances and that the sample and calibration solutions are often similar.

However, if validation criteria for analytical methods are given in the prescribed EC methods, OECD Test Guidelines or CIPAC methods, they must always be met.

4.2 Minimum validation requirement for the assessment of existing methods for risk assessment

Methods for risk assessment developed prior to the revision of this guidance often do not meet the validation requirements stated in section 4.1.4. Nevertheless, in order to reduce the need to repeat studies, especially in cases where vertebrate animals are involved, minimum validation requirements were defined for such methods to be deemed fit for the intended purpose. It should be noted that setting these minimum validation requirements does not replace expert judgement on the acceptability of a method.

For each matrix, the presented validation data should comprise at least the following parameters:

- Demonstration of linearity (calibration plot or raw data)
- Demonstration of selectivity and specificity (chromatogram of a sample at LOQ, chromatogram of blank sample)
- Demonstration of acceptable recovery (minimum of three recovery samples, with at least one of them at the LOQ level.)

Deviations from these requirements can be justified for vertebrate animal studies.

5 Validation requirements for methods for post-approval control and monitoring purposes

5.1 Analytical methods for monitoring residues in food of plant origin

5.1.1 Purpose

Analysis of food of plant origin is required to check for compliance with maximum residue levels (MRLs) [4].

5.1.2 Selection of analytes

The selection of analytes for which methods for food are required depends upon the definition of the residue for which an MRL is set or applied for according to Regulation (EC) No 396/2005.

5.1.3 Commodities and matrix groups

Methods validated according to Sections 3.1 to 3.10 must be submitted for at least one representative commodity (also called “matrix”) of all of the following matrix groups:

- dry commodities (high protein/high starch content)
- commodities with high water content
- commodities with high oil content
- commodities with high acid content

An assignment of the commodities to their respective matrix groups is presented in Appendix 1, Table A1.

If samples with high water content are extracted at a controlled pH (e.g. extraction with an acidified/basified solvent), a particular method or validation for commodities with high acid content is not required.

Where a previously validated method has been adopted to a new matrix group, validation data must be submitted for at least one representative matrix of this group.

Methods for commodities which are difficult to analyse (e.g. coffee beans, cocoa beans, herbal infusions, hops, spices, tea; see also Appendix 1, Table A1 for further examples) are only required, if authorization is requested by an applicant. Since these matrices differ strongly from each other, extrapolation between matrices is not possible. Hence, a full validation (primary method, ILV and confirmation) for that specific commodity shall be presented to prove the suitability of the method.

5.1.4 Limit of quantification

Generally, an LOQ of at least 0.01 mg/kg should be met, except for MRLs which have been established at an even lower level (e.g. for compounds with a very low toxicological reference value) which then has to be covered by the LOQ. In cases where the lowest MRL in the respective matrix group is established at a level higher than 0.01 mg/kg it is sufficient if the LOQ complies with this limit. Further information is given at Section 3.4.

5.1.5 Independent laboratory validation (ILV)

An ILV must be conducted for representative commodities of all matrix groups for which a primary method is required, with the same number of samples and fortification levels. If the primary method is identical for all matrix groups, it is sufficient to perform the ILV for commodities of two of these groups, one of them with high water content.

If a validated primary method is required for commodities difficult to analyse (Appendix 1, Table A1) an ILV must be performed for the same matrix.

If validation data for the monitoring method of an analyte in at least one of the commodities of the respective matrix group have been provided in European official standards, e.g.

- CEN/TR 17063:2018 (Modular QuEChERS), Table 1, [26]

and if these data have been generated in more than one laboratory according to the correct residue definition with the required LOQ and acceptable recovery and RSD data (see Section 3.5), additional validation by an independent laboratory is not required.

Example: An applicant seeking for authorization of a product containing active substance A in cereals provides with his application a validation of the QuEChERS method for active substance A in wheat grain. According to CEN/TR 17063:2017 (Modular QuEChERS), Table A2, the validation of active substance A was performed with wheat flour in 3 laboratories spiked at 0.01 and 0.1 mg/kg with 5 fortifications at each level, and resulted in acceptable recovery and RSD data. Therefore, the method is considered to be independently validated and an additional ILV for dry commodities (high protein/high starch content) is not required.

Additional validation data for multi residue methods have also been generated by the different laboratories and are provided in the EURL data pool. However, since the information of the validation is incomplete (e.g. no information on calibration, ion transitions etc.), the data are considered not sufficient to be used as ILV.

5.1.6 Confirmation

Confirmatory methods according to Section 3.7 must be submitted for representative commodities of all four matrix groups and difficult matrices if applicable.

5.2 Analytical methods for monitoring residues in food of animal origin

5.2.1 Purpose

Analysis of food of animal origin is required to check for compliance with MRLs [18].

5.2.2 Selection of analytes

The selection of analytes for which methods for food of animal origin are required depends on the definition of the residue for which an MRL is set or applied for according to Regulation (EC) No 396/2005.

5.2.3 Commodities

Methods validated according to Sections 3.1 to 3.10 must be submitted for the following animal matrices:

- Milk
- Eggs
- Muscle (e.g. bovine or poultry)
- Fat
- Liver or kidney (covers also edible offal)
- Honey

For honey, methods must be validated according to Section 3 with a multi-flower honey. Characteristics of the honey sample (e.g. origin of honey and pH) should be provided in the method description to support its selection. For further information on the requirement for methods please refer to SANTE/11956/2016 rev. 9 [21].

5.2.4 Limit of quantification

Generally, an LOQ of at least 0.01 mg/kg should be met, except for MRLs which have been established at an even lower level which then has to be covered by the LOQ. In cases where the lowest MRL in the respective matrix is established at a level higher than 0.01 mg/kg, it is sufficient if the LOQ complies with this limit. Further information is given in Section 3.4.

5.2.5 Independent laboratory validation (ILV)

An ILV must be conducted with samples of representative commodities from all matrices for which a primary method is required, with the same number of samples and fortification levels. If a primary method is identical for all matrices listed under Section 5.2.3, it is sufficient to perform the ILV with at least two of these matrices. This does not apply to honey where an ILV is generally required since the matrix is very different from the other animal matrices.

5.2.6 Confirmation

Confirmatory methods according to Section 3.7 must be submitted for all commodities.

5.3 Analytical methods for monitoring residues in soil

5.3.1 Purpose

Methods are required for enforcement of restrictions, post-approval control, emergency measures in the case of an accident and surveillance of buffer zones to surface waters, except in the following cases:

- Analytical methods for residues in soil are not necessary, if more than 90% of the start concentration of the active substance and its relevant metabolites are degraded within 3 days (DT_{90} < 3 d).
- Methods for naturally occurring non-toxic substances (e.g. sulphur, benzoic acid, fatty acids) are not required.

5.3.2 Selection of analytes

The residue definition for monitoring purposes in soil is based on the assessment of fate and ecotoxicology and may include the active substance and/or relevant metabolites.

For active substances which were already peer reviewed, EFSA Conclusions provide information as to which analytes are relevant for monitoring in soil.

5.3.3 Samples

Methods must be validated according to Section 3.1 to 3.7 and 3.9 with one representative soil of crop growing areas (preferably a soil with organic carbon content >1%). Characteristics of the soil sample with regard to soil type (i.e. sand, silt, clay, or loam type), pH and organic matter/carbon content should be provided in the method description to justify its selection.

5.3.4 Limit of quantification

Usually, the limit of quantification for residues in soil should be not more than 0.05 mg/kg.

If the relevant ecotoxicological concentration (ER_{50}, LC_{50}, NOEC) for the most sensitive terrestrial non-target organism is lower than 0.05 mg/kg (referring to 75 g/ha)[4] the LOQ must comply with this value.

With regard to effects on terrestrial non-target higher plants from phytotoxic herbicides, the LOQ should also comply with the lowest application rate showing 50% effect (vegetative vigour or seedling emergence/growth ER_{50}-value) in the plant tested.

[4] Expected concentrations in soil can be calculated from the application rate of an active substance (in [g a.s./ha]) using the following equation:

$$c = \frac{\text{application rate}}{\text{soil depth} \times \text{soil density}}$$

with soil depth: 10 [cm]; soil density: 1.5 [g/cm^3]

$$c = \text{application rate} \times \frac{1}{1500} \left[\frac{mg}{kg} \right]$$

Methods for highly phytotoxic compounds possibly demand highly sophisticated equipment to meet the required LOQ. Therefore, techniques that are not considered as commonly available can be accepted if justified.

5.3.5 Confirmation

Confirmatory methods according to Section 3.7 must be submitted.

5.4 Analytical methods for monitoring residues in water

5.4.1 Purpose

Methods are required for enforcement of the drinking water limit [27] or the groundwater limit [28] of 0.1 µg/L, post-approval control and emergency measures in the case of an accident, except in the following cases:

- Analytical methods for residues in water are not necessary, if more than 90% of the start concentration of the active substance and its relevant metabolites are degraded within 3 days (DT_{90} < 3 d).
- Methods for naturally occurring non-toxic substances are not required.

5.4.2 Selection of analytes

The residue definition for monitoring purposes in drinking water and surface water is based on the assessment of fate and ecotoxicology and may include the active substance and/or relevant metabolites.

For active substances that were already peer reviewed, EFSA Conclusions provide information on which analytes are relevant for monitoring in drinking water/groundwater and surface water.

5.4.3 Samples

Methods must be validated according to Section 3.1 to 3.7 and 3.9 for the following matrices:

- Drinking water or groundwater
- Surface water (freshwater, e.g. from rivers or ponds)

Provided that a method has been successfully validated for surface water at the LOQ required for drinking water (≤0.1 µg/L), no separate validation in drinking water is required.

In the method description the sampling site should be indicated. For the surface water used in method validation, quality data shall be provided to demonstrate that the sample is a typical surface water in terms of its inorganic load (e.g. conductivity, hardness, pH) and its organic load (e.g. dissolved organic carbon content (DOC)).

5.4.4 Limit of quantification

For drinking water or groundwater the limit of quantification must meet 0.1 µg/L [27]. For surface water, the LOQ should comply with the regulatory acceptable concentration (RAC*)[5], in agreement with the water framework directive 2000/60/EC [29, 30]. If no RAC* is available, the LOQ must comply with the lowest relevant ecotoxicological concentration (EC_{50}, LC_{50}, NOEC) [30] mentioned in Table 6 for the most sensitive aquatic non-target organism.

[5] If derived, RAC* values can be found in the List of Endpoints of EFSA Conclusions. See section "*Toxicity/exposure ratios for the most sensitive aquatic organisms*"

Table 6: Concentrations relevant for deriving the required LOQ in surface water

	Acute test	**Long-term test**
Fish (e.g. *Pimephales promelas*)	≤ LC_{50}	≤ NOEC
Aquatic invertebrates (e.g. *Daphnia*)	≤ EC_{50}	≤ NOEC
Sediment dwelling organisms (e.g. *Chironomus* sp)	≤ EC_{50}	≤ NOEC
Algae (e.g. *Desmodesmus subcapitata*)	≤ EC_{50}	
Higher aquatic plants (e.g. *Lemna* sp)	≤ EC_{50}	

5.4.5 Direct injection

In case HPLC-MS/MS is used, the direct injection of water samples is desirable, provided this complies with the LOQ. While recovery data cannot be calculated in this case, calibration and precision data have to be presented.

5.4.6 Independent laboratory validation (ILV)

An ILV must be conducted for drinking water or ground water (according to Section 3.8), with the same number of fortification levels and fortified samples per level as for the primary method.

5.4.7 Confirmation

Confirmatory methods for drinking/ground and surface water according to Section 3.7 must be submitted.

5.5 Analytical methods for monitoring residues in air

5.5.1 Purpose

Methods are required for monitoring of the exposure of operators, workers, bystanders and working place concentrations.

5.5.2 Selection of analytes

Analyte selection is governed by inhalation toxicity for operators, workers and/or bystanders as the primary criterion, and comprises the active substance in most cases. For active substances that were already peer reviewed, EFSA Conclusions provide information as to which analytes are relevant for monitoring in air.

Methods for naturally occurring non-toxic substances are not required.

5.5.3 Samples

Methods shall be validated according to Sections 3.2 to 3.6 and 3.9 with air at 35°C and at least 80% relative humidity (RH). In justified cases (e.g. heat sensitive analyte) and if it is shown that a method does not work at 35°C and 80% RH, other conditions are applicable (e.g. ambient temperature and normal humidity).

5.5.4 Limit of quantification

If a limit was established according to Council Directive 98/24/EC [31], the LOQ should comply with this value. With no limit in place the LOQ should comply with the concentration c calculated from the $AOEL_{inhalative}$ (in [mg/kg bw d]) according to the following equation:

$$c = AOEL_{inhalative} \times \frac{safety\ factor\ \times body\ weight}{air\ intake}$$

With safety factor: 0.1; body weight: 60 [kg]; air intake: 20 [m^3/day]

$$c = AOEL_{inhalative} \times 300\ \frac{\mu g}{m^3}$$

If no $AOEL_{inhalative}$ is available, the $AOEL_{systemic}$ or the ADI value can be used for calculation.

In case that inhalation toxicity studies show that an active substance induces local effects on the respiratory tract rather than systemic effects, the $AEC_{inhalation}$ [32] is the relevant level the LOQ has to comply with.

5.5.5 Sorbent characteristics

The sorbent used to trap airborne residues must be able to trap both gaseous and particulate materials. Two-part air sampling tubes with two separated sorbent layers must be used and both sorbent layers must be analysed separately.

5.5.6 Further validation data

The retention capacity of the sorbent material must be proven. This may be carried out by determining the recovery of the analyte, added onto the sorbent, after passage of a defined

volume of air (>100 L) for at least 6 hours at defined air temperature and relative humidity. The capacity is considered sufficient if no significant breakthrough (<10%) occurs into the secondary sorbent section of the air sampling tube.

Data to demonstrate the extractability of the analyte from the sorbent and on the storage stability conditions of the analyte loaded onto the sorbent, must be provided by way of acceptable recovery data from fortified sampling tubes.

5.5.7 Confirmatory methods

If the analytical detection technique of the method matches that used in either the soil or water, analytical methods and either of these methods demonstrate suitable confirmatory methods, no further confirmatory information is required for air methods.

5.6 Analytical methods for monitoring residues in body fluids and tissues

5.6.1 Purpose

Methods are required for detection of active substances and/or metabolites in humans and animals after possible intoxications or for biomonitoring purposes, regardless of their toxicological classification.

5.6.2 Selection of analytes

The residue definition for monitoring purposes in body fluids and tissues is based on the assessment of rodent and livestock metabolism studies and may include the active substance and/or relevant metabolites. The residue definitions might be different for body fluids and for tissues based on the assessment of the mentioned metabolism studies. For active substances that were already peer reviewed, EFSA Conclusions provide information as to which analytes are relevant for monitoring in body fluids and tissues. In the absence of an EFSA Conclusion, analytes relevant to the enforcement residue definition for animal matrices can be considered adequate also for body tissues.

5.6.3 Samples

Methods must be validated according to Sections 3.1 to 3.7 and 3.9 with the following matrix groups:

- Body fluids (either blood, serum, plasma or urine)
- Body tissues (either meat, liver or kidney)

The respective methods should be validated with the matrix which is most suitable to prove intoxication or for biomonitoring.

In contrast to Section 3.5, validation of two samples of blank matrix and 5 samples at LOQ levels is sufficient.

Suitable methods for body tissues could be available from methods for food of animal origin if the residue definition is covered.

5.6.4 Limit of quantification

The LOQ shall meet 0.01 mg/L for body fluids and 0.01 mg/kg for body tissues. Higher LOQs are acceptable for analytically challenging analytes, if justified.

5.6.5 Confirmation

Confirmatory methods according to Section 3.7 must be submitted.

6 Abbreviations

AAS	atomic absorption spectroscopy
ADI	acceptable daily intake
$AEC_{inhalation}$	adverse effect concentration for exposure by inhalation
AOAC	Association of Official Analytical Chemists
$AOEL_{inhalative}$	acceptable operator exposure level for exposure by inhalation
$AOEL_{systemic}$	acceptable operator exposure level concerning systemic effects
CEN	European Committee for Standardisation
DAD	diode array detector
DOC	dissolved organic carbon
DT_{90}	time required for 90% degradation
EC_{50}	concentration showing 50% effect
ECD	electron capture detector
EFSA	European Food Safety Authority
ER_{50}	application rate showing 50% effect
ESI	electrospray ionisation
EU	European Union
EURL	European Reference Laboratories
FID	flame ionisation detector
FLD	fluorescence detector
FPD	flame photometric detector
GC	gas chromatography
GLP	good laboratory practice
HPLC	high-performance liquid-chromatography
HRMS	high resolution mass spectrometry
ICP	inductively coupled plasma
IEC	ion exchange chromatography
IL-IS	isotopically labelled internal standard
ILV	independent laboratory validation
LC_{50}	concentration showing 50% lethal effect
LOQ	limit of quantification (here: lowest successfully validated level)
MRL	maximum residue level
MS	mass spectrometry
MS^n	multiple-stage mass spectrometry (with $n \geq 2$), including MS/MS
m/z	mass-to-charge ratio
NOEC	no observed effect concentration

NPD	nitrogen phosphorus detector
OECD	Organisation of Economic Cooperation and Development
OES	optical emission spectroscopy
PLOT	porous layer open tubular
RAC	raw agricultural commodity
RAC*	regulatory acceptable concentration
RH	relative humidity
RSD	relative standard deviation (coefficient of variation)
SRM	selected reaction monitoring
TOF	time of flight
UPLC	ultra performance liquid chromatography
UV	ultraviolet (detector)

7 References

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2. *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.*
3. *Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, 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.*
4. *Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC.*
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7. *OECD (2007) Guidance Document on Pesticide Residue Analytical Methods. OECD Environment, Health and Safety Publications, Series on Testing and Assessment No. 72 and Series on Pesticides No. 39. ENV/JM/MONO (2007) 17.*
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13. *European Committee for Standardisation (CEN) EN 12393-2:2014. Non-fatty foods. Multiresidue methods for the gas chromatographic determination of pesticide residues. Methods for extraction and clean-up.*
14. *European Committee for Standardisation (CEN) EN 12393-3:2014. Non-fatty foods. Multiresidue methods for the gas chromatographic determination of pesticide residues. Determination and confirmatory tests.*
15. *European Committee for Standardisation (CEN) EN 15662:2018. Foods of plant origin - Multimethod for the determination of pesticide residues using GC- and LC-based analysis following acetonitrile extraction/partitioning and clean-up by dispersive SPE - Modular QuEChERS-method.*
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Appendix 1: List of commodities and their respective matrix groups (adopted from EFSA PROFile 3.0)

Table A1: Assignment of food of plant origin to their respective crop group

Commodity - code	Commodity - name	Analytical method - group	Comments
110010	Grapefruit	high acid content commodities	
110020	Oranges	high acid content commodities	
110030	Lemons	high acid content commodities	
110040	Limes	high acid content commodities	
110050	Mandarins	high acid content commodities	
120010	Almonds	high oil content commodities	
120020	Brazil nuts	high oil content commodities	
120030	Cashew nuts	high oil content commodities	
120040	Chestnuts	dry commodities	
120050	Coconuts	high oil content commodities	
120060	Hazelnuts	high oil content commodities	
120070	Macadamia	high oil content commodities	
120080	Pecans	high oil content commodities	
120090	Pine nuts	high oil content commodities	
120100	Pistachios	high oil content commodities	
120110	Walnuts	high oil content commodities	
130010	Apples	high water content commodities	
130020	Pears	high water content commodities	
130030	Quinces	high water content commodities	
130040	Medlar	high water content commodities	
130050	Loquat/Japanese medlars	high water content commodities	
140010	Apricots	high water content commodities	
140020	Cherries	high water content commodities	
140030	Peaches	high water content commodities	
140040	Plums	high water content commodities	
151010	Table grapes	high acid content commodities	
151020	Wine grapes	high acid content commodities	
152000	Strawberries	high acid content commodities	

Commodity - code	Commodity - name	Analytical method - group	Comments
153010	Blackberries	high acid content commodities	
153020	Dewberries	high acid content commodities	
153030	Raspberries	high acid content commodities	
154010	Blueberries	high acid content commodities	
154020	Cranberries	high acid content commodities	
154030	Currants (red, black and white)	high acid content commodities	
154040	Gooseberries	high acid content commodities	
154050	Rose hips	high acid content commodities	
154060	Mulberries	high acid content commodities	
154070	Azarole (mediteranean medlar)	high acid content commodities	
154080	Elderberries	high acid content commodities	
161010	Dates	high water content commodities	
161020	Figs	high water content commodities	
161030	Table olives	high oil content commodities	
161040	Kumquats	high acid content commodities	High water content in PROFile 3.0, but citrus fruit, pH ~4
161050	Carambola	high acid content commodities	
161060	Kaki (Japanese persimmon)	high water content commodities	
161070	Jambolan (java plum)	high water content commodities	
162010	Kiwi	high acid content commodities	
162020	Lychee (Litchi)	high water content commodities	
162030	Passion fruit	high acid content commodities	
162040	Prickly pear (cactus fruit)	high water content commodities	
162050	Star apple	high water content commodities	
162060	American persimmon (Virginia kaki)	high water content commodities	
163010	Avocados	high oil content commodities	
163020	Bananas	high water content commodities	
163030	Mangoes	high water content commodities	
163040	Papaya	high water content commodities	
163050	Pomegranate	high acid content commodities	
163060	Cherimoya	high water content commodities	

Commodity - code	Commodity - name	Analytical method - group	Comments
163070	Guava	high water content commodities	
163080	Pineapples	high acid content commodities	
163090	Bread fruit	high water content commodities	
163100	Durian	high water content commodities	
163110	Soursop (guanabana)	high water content commodities	
211000	Potatoes	high water content commodities	
212010	Cassava	high water content commodities	
212020	Sweet potatoes	high water content commodities	
212030	Yams	high water content commodities	
212040	Arrowroot	high water content commodities	
213010	Beetroot	high water content commodities	
213020	Carrots	high water content commodities	
213030	Celeriac	high water content commodities	
213040	Horseradish	high water content commodities	
213050	Jerusalem artichokes	high water content commodities	
213060	Parsnips	high water content commodities	
213070	Parsley root	high water content commodities	
213080	Radishes	high water content commodities	
213090	Salsify	high water content commodities	
213100	Swedes	high water content commodities	
213110	Turnips	high water content commodities	
220010	Garlic	high water content commodities	
220020	Onions	high water content commodities	
220030	Shallots	high water content commodities	
220040	Spring onions	high water content commodities	
231010	Tomatoes	high water content commodities	
231020	Peppers	high water content commodities	

Commodity - code	Commodity - name	Analytical method - group	Comments
231030	Aubergines (egg plants)	high water content commodities	
231040	Okra, lady's fingers	high water content commodities	
232010	Cucumbers	high water content commodities	
232020	Gherkins	high water content commodities	
232030	Courgettes	high water content commodities	
233010	Melons	high water content commodities	
233020	Pumpkins	high water content commodities	
233030	Watermelons	high water content commodities	
234000	Sweet corn	high water content commodities	
241010	Broccoli	high water content commodities	
241020	Cauliflower	high water content commodities	
242010	Brussels sprouts	high water content commodities	
242020	Head cabbage	high water content commodities	
243010	Chinese cabbage	high water content commodities	
243020	Kale	high water content commodities	
244000	Kohlrabi	high water content commodities	
251010	Lamb's lettuce	high water content commodities	
251020	Lettuce	high water content commodities	
251030	Scarole (broad-leaf endive)	high water content commodities	
251040	Cress	high water content commodities	
251050	Land cress	high water content commodities	
251060	Rocket, Rucola	high water content commodities	
251070	Red mustard	high water content commodities	

Commodity - code	Commodity - name	Analytical method - group	Comments
251080	Leaves and sprouts of Brassica spp	high water content commodities	
252010	Spinach	high water content commodities	
252020	Purslane	high water content commodities	
252030	Beet leaves (chard)	high water content commodities	
253000	Vine leaves (grape leaves)	high water content commodities	
254000	Water cress	high water content commodities	
255000	Witloof	high water content commodities	
256010	Chervil	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256020	Chives	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256030	Celery leaves	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256040	Parsley	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256050	Sage	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256060	Rosemary	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256070	Thyme	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256080	Basil	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
256090	Bay leaves (laurel)	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult

Commodity - code	Commodity - name	Analytical method - group	Comments
256100	Tarragon	high water content commodities	The fresh commodity is considered as high water content, while the dried commodity is considered difficult
260010	Beans (fresh, with pods)	high water content commodities	
260020	Beans (fresh, without pods)	high water content commodities	
260030	Peas (fresh, with pods)	high water content commodities	
260040	Peas (fresh, without pods)	high water content commodities	
260050	Lentils (fresh)	high water content commodities	
270010	Asparagus	high water content commodities	
270020	Cardoons	high water content commodities	
270030	Celery	high water content commodities	
270040	Fennel	high water content commodities	
270050	Globe artichokes	high water content commodities	
270060	Leek	high water content commodities	
270070	Rhubarb	high acid content commodities	
270080	Bamboo shoots	high water content commodities	
270090	Palm hearts	high water content commodities	
280010	Cultivated fungi	high water content commodities	
280020	Wild fungi	high water content commodities	
290000	Sea weeds	high water content commodities	
300010	Beans (dry)	dry commodities	
300020	Lentils (dry)	dry commodities	
300030	Peas (dry)	dry commodities	
300040	Lupins (dry)	dry commodities	
401010	Linseed	high oil content commodities	
401020	Peanuts	high oil content commodities	
401030	Poppy seed	high oil content commodities	
401040	Sesame seed	high oil content commodities	
401050	Sunflower seed	high oil content commodities	
401060	Rape seed	high oil content commodities	
401070	Soya bean	high oil content commodities	

Commodity - code	Commodity - name	Analytical method - group	Comments
401080	Mustard seed	high oil content commodities	
401090	Cotton seed	high oil content commodities	
401100	Pumpkin seeds	high oil content commodities	
401110	Safflower	high oil content commodities	
401120	Borage	high oil content commodities	
401130	Gold of pleasure	high oil content commodities	
401140	Hempseed	high oil content commodities	
401150	Castor bean	high oil content commodities	
402010	Olives for oil production	high oil content commodities	
402020	Palm nuts (palmoil kernels)	high oil content commodities	
402030	Palmfruit	high oil content commodities	
402040	Kapok	high oil content commodities	
500010	Barley grain	dry commodities	
500020	Buckwheat grain	dry commodities	
500030	Maize grain	dry commodities	
500040	Millet grain	dry commodities	
500050	Oats grain	dry commodities	
500060	Rice grain	dry commodities	
500070	Rye grain	dry commodities	
500080	Sorghum grain	dry commodities	
500090	Wheat grain	dry commodities	
610000	Tea (dried leaves and stalks, fermented or otherwise of Camellia sinensis)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
620000	Coffee beans	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
631000	Herbal infusions (dried, flowers)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
632000	Herbal infusions (dried, leaves)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
633000	Herbal infusions (dried, roots)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
640000	Cocoa (fermented beans)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
650000	Carob (St Johns bread)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops

Commodity - code	Commodity - name	Analytical method - group	Comments
700000	Hops (dried), including hop pellets and unconcentrated powder	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
810000	Spices (seeds)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
820000	Spices (fruits and berries)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
830000	Spices (bark)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
840000	Spices (roots and rhizome)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
850000	Spices (buds)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
860000	Spices (flower stigma)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops
870000	Spices (aril)	difficult	“No group” in PROFile 3.0, but considered “difficult” here due to high matrix load of these crops

Commodity - code	Commodity - name	Analytical method - group	Comments
900010	Sugar beet (root)	high water content commodities	
900020	Sugar cane	high water content commodities	
900030	Chicory roots	high water content commodities	

Table A2: Assignment of feed to their respective crop group (if not already mentioned in Table A1)

Commodity - name	Analytical method - group	Comments
Forages (e.g. alfalfa, barley, clover, grass, maize, millet, oat, rye, triticale, wheat)	high water content commodities	
Hays (e.g alfalfa, clover, grass, oat,	dry commodities	
Straws (e.g.barley oat, rye, wheat	dry commodities	“No group” in PROFile 3.0, but considered dry here
Stovers (e.g.maize)	dry commodities	
Silages (e.g. alfalfa, clover, grass, maize)	high water content commodities	
Vines (e.g. bean, pea)	high water content commodities	
Leaves or tops (e.g. fodder beet, sugar beet, turnip)	high water content commodities	
Roots (fodder beet)	high water content commodities	
Grains and seeds (e.g. cowpea)	dry commodities	
Apple pomace	high water content commodities	

Table A3: Assignment of processed commodities to their respective crop group

Raw Agricultural Commodity (RAC)	Processed Commodity	Commodity category
Bananas	RAC	high water content
	fruit, dried	dry / high sugar content
Barley	RAC	dry
	beer	high water content
	bran	dry
	brewer's grain	high water content
	flour	dry
	grits	dry
	malt	dry
	pot/pearl barley	dry
Beans, fresh	RAC	high water content
	pod, canned	high water content
	pod, cooked	high water content
	seed, canned	high water content
	seed, cooked	high water content
Carrots	RAC	high water content
	juice	high water content
	peel	high water content
	pomace, wet	high water content
	root body, canned	high water content
	root body, cooked	high water content
Cauliflowers	RAC	high water content
	head, cooked	high water content
Citrus fruits (grapefruits, lemons, limes, mandarins, oranges)	RAC	high acid content
	concentrate	high acid content
	fruit, canned	high acid content
	juice	high acid content
	marmalade	high water content
	oil	high oil content
	pomace, wet	high acid content
	pulp	high acid content
	pulp, dried	high acid content
Cocoa beans	RAC	difficult
	cocoa butter	difficult
	cocoa mass	difficult
	cocoa powder	difficult
	cocoa press cake	difficult
Coffee beans	RAC	difficult
	coffee bean, roasted	difficult
	instant coffee	difficult
Cotton seeds	RAC	high oil content
	extracted meal	dry
	hulls	dry
	oil	high oil content
	pressed cake	high oil content
Currants	RAC	high acid content
	fruit, canned	high acid content
	fruit, cooked	high acid content
	jam	high water content
	jelly	high water content
	juice	high acid content
Gherkins	RAC	high water content
	fruit, canned	high acid content
	fruit, cooked	high water content
	fruit, fermented	high acid content

Raw Agricultural Commodity (RAC)	Processed Commodity	Commodity category
Head cabbage	RAC	high water content
	head, cooked	high water content
	sauerkraut juice	high acid content
	sauerkraut	high acid content
Herbal infusions	RAC	high water content
	dried	difficult
	leaves/flowers/seeds	high water content
	infusions	
Hops	RAC	difficult
	beer	high water content
	hops extract	difficult
	spent hops	difficult
Leeks	RAC	high water content
	vegetable, cooked	high water content
Linseed	RAC	high oil content
	oil	high oil content
	extracted meal	dry
	pressed cake	high oil content
Maize	RAC	dry
	extracted meal	dry
	flour	dry
	grits	dry
	oil	high oil content
	pressed cake	high oil content
	starch	dry
Melons	RAC	high water content
	pulp	high water content
Oats	RAC	dry
	flour	dry
	rolled oats	dry
Olives (Table olives and olives for oil production)	RAC	high oil content
	extracted meal	dry
	fruit canned	high oil content
	fruit fermented	high oil content
	oil	high oil content
	pomace, wet	high oil content
Onions	RAC	high water content
	bulb, dried	dry
Papayas	RAC	high water content
	pulp	high water content
Passion fruits	RAC	high acid content
	pulp	high acid content
Peanuts	RAC	high oil content
	extracted meal	dry
	oil	high oil content
	peanut butter	high oil content
	pressed cake	high oil content
	roasted peanuts	high oil content
Peas, fresh	RAC	high water content
	pod, canned	high water content
	pod, cooked	high water content
	seed, canned	high water content
	seed, cooked	high water content
Pineapple	RAC	high acid content
	juice	high acid content
Pome fruits (Apples, Pears)	RAC	high water content
	fruit, canned	high water content
	fruit, dried	dry / high sugar content
	jelly	high water content
	juice	high water content
	pomace, wet	high water content
	pulp	high water content
	purée	high water content

Raw Agricultural Commodity (RAC)	Processed Commodity	Commodity category
Potatoes	RAC	high water content
	crisps	high oil content
	flakes/granules	dry
	peel	high water content
	peel, dried	dry
	pulp	high water content
	pulp, dried	dry
	starch	dry
	tuber, baked	high water content
	tuber, cooked	high water content
	tuber, deep-fried	high oil content
Pulses (Beans, Peas)	RAC	dry
	seed, canned	high water content
	seed, cooked	high water content
Rapeseed	RAC	high oil content
	extracted meal	dry
	oil	high oil content
	pressed cake	high oil content
Rice	RAC	dry
	rice, polished	dry
Rye	RAC	dry
	bran	dry
	flour	dry
Sorghum	RAC	dry
	flour	dry
	starch	dry
Soybeans	RAC	high oil content
	extracted meal	dry
	hulls	dry
	oil	high oil content
	pressed cake	high oil content
	soya drink	high water content
	soya sauce	high water content
	tofu	high water content
Spinaches	RAC	high water content
	leaves, cooked	high water content
Stone fruits (Apricots, Cherries, Peaches, Plums)	RAC	high water content
	fruit, canned	high water content
	fruit, cooked	high water content
	fruit, dried	dry / high sugar content
	jam	high water content
	juice	high water content
	pulp	high water content
	purée	high water content
Strawberries	RAC	high acid content
	fruit canned	high acid content
	fruit cooked	high acid content
	jam	high water content
	juice	high acid content
	pulp	high acid content
Sugar beet root	RAC	high water content
	molasse	dry / high sugar content
	pulp, dried	dry
	sugar, refined	dry / high sugar content
Sugar cane	RAC	high water content
	molasse	dry / high sugar content
Sunflower seeds	RAC	high oil content
	extracted meal	dry
	oil	high oil content
	pressed cake	high oil content

Raw Agricultural Commodity (RAC)	Processed Commodity	Commodity category
Table and wine grapes	RAC	high acid content
	jelly	high water content
	juice	high acid content
	must	high acid content
	oil	high oil content
	pomace, wet	high acid content
	raisin	dry / high sugar content
	spirit	high water content
	wine	high acid content
Tea	RAC	difficult
	dried, fermented	difficult
	brewed tea	high water content
Tomatoes	RAC	high water content
	fruit, canned	high water content
	fruit, cooked	high water content
	fruit, dried	dry
	juice	high water content
	paste	high water content
	pomace, wet	high water content
	purée	high water content
Wheat	RAC	dry
	bran	dry
	flour	dry
	germs	dry
	gluten	dry
	gluten feed meal	dry
	grits	dry
	malt	dry
	starch	dry

Appendix 2: List of methods required

Table A2: Completeness check of analytical methods for post-approval control and monitoring purposes

Matrix group / crop group	Residue definition for monitoring	LOQ	Methods		
			Primary method	Confirmatory method	Independent lab validation
Dry commodities (high protein/high starch content)					
Commodities with high water content					
Commodities with high oil content					
Commodities with high acid content					
Commodities which are difficult to analyse					
Milk					
Eggs					
Meat					
Fat					
Kidney/liver					
Honey					
Soil					Not necessary
Drinking water					
Surface water					Not necessary
Air					Not necessary
Body fluids					Not necessary
Body tissues					Not necessary