

September 2026

Guidance on the Conduct of Dislodgeable Foliar Residue (DFR) Studies

Developed by: Crop Life Europe Occupational and Bystander Exposure Technical Sub-Group (OBE TSG)

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Abstract

Worker-, Bystander- and Resident-Exposure are mainly or partly originating from contact of body parts with crop foliage treated with plant protection products (PPP, products). Therefore, knowledge about the amount of residue that can be dislodged from crop surfaces is important to estimate potential exposure upon re-entry activities. This can be determined with Dislodgeable Foliar Residue (DFR) studies.

The purpose of this guidance is to outline the principles and considerations for conducting DFR studies in a scientifically robust and representative manner and to help harmonise study procedures and interpretation without interfering with individual study purposes.

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Guidance Source Material

This guidance document was developed by the CropLife Europe Occupational and Bystander Exposure Technical Sub-Group (CLE OBE TSG).

The study design, data generation and data analysis/processing detailed in this document were developed in an attempt to standardize measurement and assessment of dislodgeable residues from crop leaves or leaf material, as a result of recommendations from EFSA [Appendix J - EFSA Journal 2022;20(1):7032].

Other guidance documents / guidelines were also consulted:

- US EPA: Occupational and Residential Exposure Test Guidelines. OPPTS 875.2100 Foliar Dislodgeable Residue Dissipation (EPA 712-C-96-267) – Feb 1996.
- Health Canada PMRA: Estimating Dislodgeable Foliar Residues and Turf Transferrable Residues in Occupational and Residential Postapplication Exposure Assessments - SPN2014-02 – Nov 2014.
- California EPA: Guidance for Determination of Dislodgeable Foliar Residues – Report HS-1600 Rev. No. 1 – Feb 2002.
- Northern Zone Steering Committee (NZSC): Guidance document on work-sharing in the Northern zone in the authorisation of PPPs, Version 14 - June 2026.
- Ministerio de Sanidad (Spain): Evaluación del riesgo por exposición a productos fitosanitarios, Versión-05; 30/03/2026.
- FOCUS, 2014: Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. FOCUS Work Group on Degradation Kinetics, Version 1.1. - 18 December 2014
- EFSA, 2019. European Food Safety Authority, 2019. Technical report on the outcome of the Pesticides Peer Review Meeting on general recurring issues in ecotoxicology. EFSA Supporting publication 2019: EN-1673. 117 pp.
- EFSA, 2014. European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662, 37 pp.

Combined expertise and experience of the CLE OBE TSG members in conducting and/or monitoring DFR studies also contributed to build this document.

Any changes in DFR study design and operation proposed in this document (when compared to previous approaches) does neither invalidate existing DFR studies nor the resulting DFR and DT₅₀ values derived.

Introduction

Worker-, Bystander- and Resident-Exposure are mainly or partly originating from contact of body parts with crop foliage either directly treated with plant protection products (PPP, products) or having received contamination by spray drift. Therefore, knowledge about the amount of dislodgeable residues remaining on crop surfaces following spray applications is an important parameter to estimate the potential exposure of workers, bystanders or residents.

Dislodgeable Foliar Residue (DFR) studies are designed and conducted to quantify the amount of pesticide residue that can be removed from plant surfaces following PPP applications. The purpose of this guidance is to outline the principles and considerations for conducting DFR studies in a scientifically robust and representative manner and to help harmonise study procedures and interpretation without interfering with individual study purposes.

In this guideline on how to conduct DFR studies, the following topics are covered.

Field phase - Trial sites and plots

- Number of trials and zonal split
- Number of plots and subplots
- Plot size and layout

Field phase - Application details

- Selection of application equipment
- Number and interval of applications
- Application timing
- Dose rate and spray volume
- Monitoring of environmental conditions
- Tank mixture sampling

Field phase - Leaf sampling, processing and storage

- Leaf sampling options
- Leaf sample collection
- Leaf sampling schedule
- Number of replicates per sample
- Leaf sample processing and storage
- Field phase - Field fortifications
- Control wash solution preparation
- Fortification solutions
- Timing of fortification experiments
- Levels of field fortifications
- Identification, handling, storage and shipment of samples

- Analysis of field fortification samples

Data reporting and adjustment for field fortification recoveries

- Residue data presentation in a study report
- Exclusion of outliers
- Consideration of recoveries

DFR and DT₅₀ derivation

- DFR Derivation
- Statistical approach
- Definitions of default DFR (DFR_{DEF}), DFR₀, DFR_X and DFR_{NORM}
- Using DFR values in risk assessment
- DT₅₀ Derivation
- Number of data points
- Data pre-processing
- Multiple applications
- Identification of the appropriate model
- Weather conditions

For the use of DFR study data in a regulatory context, it is recommended to follow internationally accepted quality criteria such as the OECD (1998), OECD Principles on Good Laboratory Practice, OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, No. 1, OECD Publishing, Paris, <https://doi.org/10.1787/9789264078536-en> and all related OECD publication on GLP compliance, which can be found on the OECD website ([OECD Principles on Good Laboratory Practice | OECD](#)).

For national or regional data use, there might be additional GLP requirements, which need to be taken into account when designing a DFR study and generating a respective study plan for data generation.

This document also encourages experts analysing DFR data to consider all available data in a scientific manner and applying expert judgement, instead of treating recommendations as strict rules.

As this document focuses on dislodgeable foliar residue (DFR) studies to mainly evaluate worker, bystander and resident exposure arising from agricultural uses of pesticides, it is considered appropriate to mention that similar studies are conducted for human exposure towards turf residues (Transferable Turf Residues – TTR) to evaluate e.g., the potential exposure of children playing on lawns, golfers, sports-field users, or turf maintenance workers.

Although there are similarities to DFR studies, especially in the study design, there are also dissimilarities in the sampling approach, where DFR quantifies what is removable from foliage, whereas TTR quantifies what can actually be transferred to cloth, skin surrogate, clothing surrogate, etc. by contact with turf.

In addition, there are specific studies to evaluate the transfer of residue from cotton material other than leaves (e.g., cotton bolls, lint, bracts) which are handled by agricultural workers and may result in dermal

exposure. These boll transferable residue (BTR) studies also have similarities to DFR studies in the study design, but also focus on the amount of residue that can be transferred from the mentioned crop components to worker matrices such as cotton gloves, cotton cloth, hands (via hand wash methodology) or other collector materials.

It is recommended that future revisions of the current document should add specific appendices to cover these two study types for the evaluation of the respective potentially exposed population groups.

Dislodgeable Foliar Residue (DFR) Guidance

1. Field phase - Trial sites and plots

1.1. Trial sites

A field trial site can be defined as a single geographical location comprising plots and/or subplots where product application and DFR sampling are performed. Field trial sites should be selected in regions representative of crop varieties and growing conditions in the intended use areas.

If the intended use is relevant for Europe, the NEU/SEU zonal split proposed in [SANTE/2019/12752 Rev02 (June 2025)] is a sufficient divide, with trials performed in each zone considered representative for all other countries within that zone (see Figures 1 and 2).

For intended uses outside of Europe trials may be distributed according to local guidance if applicable. However, geographical locations should be selected to reflect the growing systems and/or weather conditions of the intended use. If trials are conducted in the same country, it is recommended that trial sites are located at least 20 km apart and that growing conditions are different (e.g., different crop variety, soil type, growing system) [SANTE/2019/12752 Rev02 (June 2025)].

Residue Regions



Figure 1: Zonal split of Europe [according to SANTE/2019/12752 Rev01 (May 2023)]

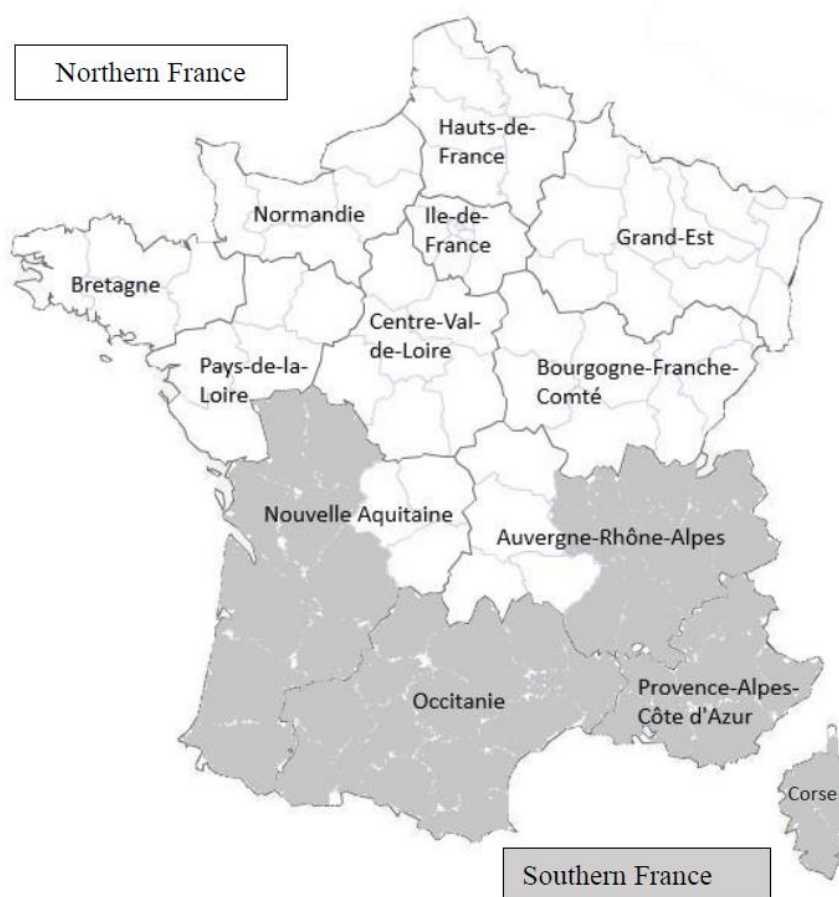


**Figure 2: Zonal split of France as part of the split of Europe
[according to SANTE/2019/12752 Rev01 (May 2023)]**

At each field trial site, one or several field plot(s) can be considered. A field plot is a defined surface area within a trial from which specimens will be taken and will be identified for the duration of the trial using stakes or canes at each corner, with relevant identification. Each plot will be of a sufficient size to sample the necessary numbers of samples.

A field plot can be an untreated (control) plot or a treated plot. A control plot will receive no treatment, whereas a treated plot will receive the test item (as described in **Section 2. Field phase - Application Details**).

A subplot is an area defined within a treated plot. Applications can be done as one operation over the whole plot (i.e., treat all subplots in the same run) or separately for each subplot.

It is recommended to take photos of the trial site and foliage at each application event and to keep these in the raw data.

1.2. Number of trials and zonal split

The number and selection of trial locations shall be determined based on the intended uses specified in the GAP. For example, in Europe:

- Crop group use(s) in NEU and SEU require: Min. 1 NEU + 1 SEU per formulation per crop group
- Crop group use(s) in NEU or SEU require: 2 NEU or 2 SEU per formulation per crop group

The term 'crop group', is considered specifically for DFR purposes and does not have a harmonised globally accepted definition. For the purposes of this guidance, crop group is defined as crops with similar leaf morphology and crop architecture (e.g., low or high crop), and expert judgement is necessary to justify the grouping and application of DFR from similar crops. Crop grouping refers to the dislodgeability of residues from treated leaves which may be defined by similar surface properties like smooth, waxy, hairy or similar wettability properties, and not merely on crop variety, species, genus, family, order, etc.

1.3. Number of plots (and subplots)

Two approaches can be supported for plot layout and sampling, with either subdivision of plots to subplots for sampling or by repeated replicate sampling throughout the total plot. Both are valid ways of sampling and can be adjusted on a case-by-case basis.

- In case of subplots, one subplot gives one replicate sample.
- In case of sampling across the complete plot, one crossing of the total plot gives one replicate sample.

The approach of collecting replicates in different parts of the plot (in subplots or crossing the total plot) addresses the inherent variability of spray deposition on foliage, which could be at various points in time impacted by spray quality, direction, terrain, etc.

A control/untreated plot should also be included along with the treated plots, resulting in: **1 C** (control) plot and at least **1 T** (treated) plot, where the T plot(s) could be subdivided in **T1, T2, T3, ...** subplots, with the number of subplots equalling the targeted number of replicates per sampling timing. In some cases, it may be possible to take control samples from the treated plot area before treatment has occurred, however, this approach should only be considered for single applications and short sampling periods. It is worth noting that this approach (not using untreated plots) limits the opportunity to investigate in-field maintenance activities and crop matrix effects as the crop matures. If additional treated plots are included to test, for example, another GAP or a piece of technology, then the same control samples can be used to support multiple treated plots as long as the treated plots are present on the same site.

Control plots should be upslope (if applicable), upwind [of application(s)] and at least 20 m away from the treated plot(s) and neighbouring fields, to reduce the potential for contamination due to drift. The crop variety, soil and environmental conditions should be the same in control and treated plots. The 20 m buffer zone could be increased for applications that generate high drift, such as airblast applications to high trees.

1.4. Plot size

Minimum number of individual plants for sampling (i.e., for trees, vines, bushes, high fruiting vegetables) or minimum size/sampling area (i.e., for row crops, broad acre crops) per plot/subplots is defined depending on the number of sampling events.

Depending on the test system and mode of application, plot borders may be required and should be defined in field layout sketches. Application must include the border rows/plants (depending on the test system fully or partly treated). However, sampling should not be conducted on any border row/plant.

For individual plants/trees, sampling shall not be done on border trees. The total number of treated plants/trees may vary depending upon the individual plant/tree dimensions, plot shape and application equipment used.

Examples of plot designs are illustrated in Appendix A -

2. Field phase - Application details

2.1. Application equipment

For the experimental setup of the DFR study it may not be possible/practical to use large-scale equipment (e.g., vehicle-mounted air-blast due to only a few tree plants treated), relevant substitute equipment should be used, providing the spray deposition is representative of a commercial agricultural application. Care should be taken to mimic the commercial application technique as much as possible and to ensure that spray deposit distribution follows the anticipated spray pattern. Therefore, consultation with the grower or regional agricultural consultant (e.g., agronomist, spray contractors) is recommended prior to conducting spray applications with surrogate equipment in DFR studies. Additionally, the selected spray operator needs to be familiar with the surrogate equipment used in the study.

Calibration should be performed at least once before the first application but may not be mandatory to repeat if the same equipment is used for further applications in the same trial. A target test item application rate of $\pm 10\%$ is preferable.

2.2. Formulation requirements and extrapolation

It is not considered practical to run DFR studies for every formulation on every crop type. Therefore, DFR data bridging is considered appropriate for formulations based on the same formulation "carrier system" if the active ingredient is the same. There are two possible carrier systems available, water-based and organic solvent-based. This approach is analogous to the 2017 EFSA dermal absorption guidance approach to default dermal absorption setting (<https://doi.org/10.2903/j.efsa.2017.4873>), crop field trial guidance OECD TG 509 (2021), as well as evidence from Maclachlan D. J. Et al 2010 (<https://doi.org/10.1080/19440040903403024>).

- **Water-based formulations:** including liquid water-based products (e.g., SC, SL) and solid formulations intended to be diluted/dispersed in water prior to application (e.g., WP, WG, SG) may be extrapolated between one another, provided the active substance is identical and the use conditions are comparable.
- **Solvent-/oil-based formulations** (e.g., EC, EW, SE and other non-aqueous or oil/solvent carrier systems) may likewise be extrapolated between one another, provided the active substance is identical and the use conditions are comparable.

Bridging between different carrier systems may be acceptable in cases where the weight of evidence or additional study data shows comparable DFR behaviour between the formulation types, following expert judgement.

2.3. Number of applications - Interval between applications

There are two main approaches to design and conduct a DFR study – a single application approach and a multiple application approach. For studies supporting single application uses a single application approach is recommended. For studies supporting multiple application uses there are two different approaches to study design and conduct:

- Conduct a DFR study with a single application and respective sampling as outlined in **Section 3. Field phase - Leaf sampling, processing and storage** of this document. The corresponding risk assessment for this product will then require the use of normalised DFR values (DFR_{NORM}) and measured or default DT_{50} values to derive a multiple application factor (MAF). This approach allows the user to model the expected DFR for any GAP including multiple applications, details on how to do this are provided in **Section 7.3. Using DFR values in risk assessment**.
- Conduct a DFR study with the maximum number of applications and the shortest interval as outlined in the product GAP and respective sampling as outlined in **Section 3. Field phase - Leaf sampling, processing and storage** of this document. The corresponding risk assessment for this product will then be typically based on the DFR_X measurement (see **Section 7.3**) (DFR value derived following the last application of the application regime). This approach covers any potential residue accumulation over multiple applications. In this case normalisation and MAFs are not included in the risk assessment because these are built into the DFR_X value.

2.4. Application timing

For study designs with more than one application of the product, the timing of applications should bracket the time frames (or growth stages) set out in the GAP. However, the timeframe of application and DFR sampling should be biased towards the later stages of the crop (i.e., higher foliage development/canopy density) to cover the worst-case scenarios of re-entry exposure for the target crop / GAP combination.

2.5. Dose rate – Spray volume

Based on the GAP, the highest product dose rate should be used for the respective application timing with an appropriate spray volume taking into account the size of the crop, equipment used, field conditions, etc.

If dose and/or volume rate(s) are planned to change during the trial, the following list must be modified accordingly, or the application schedule can be presented in a distinct table.

The minimum information required in a DFR Study Plan is:

- **Number of applications.**
- **Application interval**, number of days between applications.
- **Timing of application**, typically a growth stage and should be selected at a typical time for crop re-entry.
- **Spray volume range**, should be appropriate for the crops present at the trial site, however applied spray volumes should be covered by the range provided in the GAP (e.g., 100 – 500 L/ha)
- **Application method**, e.g., foliar application with horizontal / vertical boom, commercial air assisted sprayer, backpack/knapsack sprayer (air assisted, pressurized, hand wand, battery operated, etc.).

2.6. Record of environmental conditions

From 24 hours before the first application day to the last sampling day, **rainfall** will be recorded on-site using a rain gauge or other appropriate equipment, with readings to be recorded prior to each DFR sampling event. Records will include, as a minimum, the date and time of reading and the volume of rain measured by the device. Where possible it would also be advantageous to record the duration of each rainfall event.

Air temperature, relative humidity, wind speed and direction will be recorded at each application event and at each sampling timing. Other conditions like BBCH crop stage and crop height will also be recorded at each application or sampling occasion.

In addition to in-field monitoring of climate conditions, air temperature and rainfalls could be recorded from the nearest weather station (the distance between the treated plot and the source of the weather data shall be recorded) or from a weather data provider covering the whole trial period at each trial site. Recording of historical data over the last 3 years is optional.

2.7. Tank mixture sampling

Tank mix samples are potentially useful to address concerns over data inconsistencies. However, compulsory analysis of tank mixtures to verify spray concentrations is not considered necessary for DFR studies. The amount of product and water and the mixing methodology used to create the tank mix will be clearly documented in the field phase of the report, therefore tank mix concentrations can be calculated and reported. Additionally, DFR trials are performed with commercial products that require tank mix stability and homogeneity testing, so tank mix solutions can be assumed to be homogeneous.

In the cases where the Study Director decides to collect tank mix samples, sampling is only recommended just after tank mix preparation and appropriate stirring before application and/or after application, not during treatment.

As homogeneity investigation of the tank mix solution is one of the purposes of tank mix sampling, it is recommended to collect at least three replicates at each sampling timepoint. The respective samples should be collected directly from the spray tank. Depending on the spraying equipment used, the procedure to collect these samples may differ and should therefore be clearly described in the study report.

Tank mix samples (approx. 20 mL each) should be stored in appropriate containers. Adsorption of a.s. on the container material should be checked before the field phase at the analytical test site, additives may need to be added to prevent a.s. degradation.

Tank mix samples will be treated as separate specimens in the field. They will be stored frozen and sent to the analytical test site along with the field study samples. It is recommended that tank mix samples are stored separately from field samples to minimise the risk of contamination. Samples will be homogenised at the analytical test site and then an aliquot from each sample will be taken.

Additionally, it is recommended to obtain a sample of the water used to generate the respective tank mix to enable the analytical chemist to investigate a potential influence of the mixing water on the spray solution in case of unexpected analytical results.

3. Field phase - Leaf sampling, processing and storage

3.1. Leaf sampling options

The untreated (control) plot should be sampled prior to the treated plot to minimize the risk of cross contamination.

There are mainly 2 options to obtain leaf material from the trial plots.

- Leaf punch, which cuts a defined number of standard sized leaf discs from intact healthy leaves of the trial plots. This procedure is the standard procedure to obtain leaf material in a DFR study. Only in the case that the leaf size or shape does not allow leaf discs to be obtained should option 2 be applied (i.e., cereals, olives, crops at early growth stages, ...)
- Whole leaf sampling, a defined number of entire leaves can be taken from the trial plots. In this case the surface area of the collected leaves should be measured and be $>400 \text{ cm}^2$ - taking into account both sides of the leaf surface.

As outlined above, sampling leaf material is typically performed by using a leaf puncher with a 1-inch punch diameter. There are other leaf punchers available (i.e., ½ -inch diameter), but in the case that the target leaves are too small for 1-inch leaf punching, the preferred approach of collecting leaf material is sampling entire leaves.

The standard approach to collect leaf material for DFR determination is to obtain a composite sample of 40 leaf discs from each plot (control plot(s) and each subplot of the treated plot(s)). Collecting 40 leaf discs of 1 inch (2.5 cm) diameter results in a total surface area (upper and lower leaf disc sides) of the sample of $2 * \pi * r^2 * 40 \sim 400 \text{ cm}^2$.

Leaf discs should be collected from the central part of leaves whenever possible. A 1-inch diameter is preferred over smaller sizes because this provides more intact surface area relative to the circumference where cells are disrupted during cutting. Gravimetric determination is not necessary when a leaf puncher can be used. Reliable measures should be applied to ensure the correct number of leaf discs has been collected.

In the case of collecting entire leaves, a surface area / weight correlation factor needs to be determined prior to collecting leaf material for DFR determination. This can be achieved by using a commercial leaf area meter or by scanning a given number of entire leaves with a flatbed scanner, and the subsequent determination of the surface with respective software (i.e., ImageJ, [ImageJ Common](#)). In both cases, the derived leaf surface area is subsequently correlated to the leaf material weight and the number of leaves collected to derive a surface area / weight correlation factor and an average surface area / leaf number correlation factor. These are subsequently used to calculate the total number of leaves to be collected to obtain a surface area (double sided) of at least 400 cm^2 . Should the number of entire leaves be significantly less than 40 to derive the 400 cm^2 area (i.e., cereal leaves), consideration should be given to the option to increase the number of entire leaves collected to ensure proper randomized sampling throughout the plots. Alternatively, the entire leaves could be reduced in size (cutting in half) to maintain 40 sampling points but reduce the area for dislodging.

Whatever option is chosen, the final determination of the area used to perform the dislodging of leaf material is to be made by weighing the leaf material prior to dislodging and calculating the dislodged area using the surface area / weight correlation factor. Finally, if a larger leaf area surface is collected the volume of dislodging solution used to dislodge the leaf material should be adopted in a pro-rata approach to approximately match the $200 \text{ mL} / 400 \text{ cm}^2$ (double sided) ratio applied in the leaf disc approach. For sampling regimens over a longer period of time, the leaf area/weight ratio determination may have to be repeated to account for mass / surface changes due to plant growth.

3.2. Leaf sample collection

Leaf material samples are to be taken from the areas of the crop canopy where contact of workers with the treated foliage is expected. The researcher needs to consider the total number of collection points (min. 40) when choosing an appropriate randomized sampling scheme.

The leaf material sampling procedure does mainly depend on the crop and production type. The following list outlines the major crop / production type situations and the proposed leaf material sampling approaches, which apply for both leaf discs and entire leaves sampling.

- **Field crops:** a standard randomization procedure such as stratified random sampling or transect sampling should be applied to obtain leaf material from all areas of the plots and to account for outer and inner plant canopy areas of the respective crops. When choosing a randomization

scheme, the expected worker re-entry activities also should be given consideration in selecting the appropriate sampling scheme.

- **Trellised crops / Row crops (trellised orchards / trellised vines):** stratified randomized collection of leaf material from both sides of the rows and from low / middle / high areas of the plants as well as from outer and inner plant foliage with focus on main foliage areas in contact during expected worker re-entry activities.
- **High crops / Individual plants (individual tree orchards, vines, bushes):** For such crops, the sampling approach by Iwata (1)¹ where samples are collected at 45-degree intervals around the circumference of each sampled tree / plant and at varying heights in the tree is proposed by several guidance documents and should be applied.

Leaf material for DFR determination will be taken when the foliage is dry. This is expected to happen not later than 4 hours after an application for the first sampling post-application.

Details on the applied randomized sampling procedure must be added to the study raw data, possibly including a sampling diagram.

The procedure for taking leaf disc or whole leaf samples should be consistent at each sampling event and should be fully documented in the field raw data. Only healthy fully expanded leaves of similar size should be sampled. Each leaf should only be sampled once.

When sampling leaf material via leaf discs, a leaf puncher should be used with a jar fitted to the leaf puncher, so that leaf discs fall directly into the jar.

When sampling leaf material as entire leaves, the opening of the sampling container must be large enough for direct collection with no contact between the sampled leaves and the outside of the container or a potential manual transfer of the cut leaves into the containers. Each sampling jar will be appropriately identified and closed with a plastic lid after sampling.

Whole leaf samples must be collected into appropriate pre-weighed containers to enable determination of the leaf material weight.

3.3. Leaf sampling schedule

The leaf sampling schedule should reflect the expected decline of surface residues (product / active substance specific) such that sufficient samples are taken at the major time of decline to accurately model the rate of decline and to derive an appropriate DT_{50} value (see **Section 8. DT_{50} derivation**).

In case of multiple applications, samples should be taken prior to and after each application on the day of application, and potentially also on additional occasions between applications, depending on the application interval and product / active substance specific degradation patterns. A typical sampling scheme for products

¹ Iwata Y, Knaak JB, Spear RC and Foster RJ, 1977. Worker re-entry into pesticide treated crops. I. Procedures for the determination of dislodgeable pesticide residue on foliage. Bulletin of Environment Contamination and Toxicology, 18, 649

with unknown degradation patterns is sampling at 0, 1, 3, 5, 7, 10, 14, 21, 28, ... DALA (days after last application).

3.4. Number of replicates per sampling

At least three replicates in each treated plot (collected either across the entire treated plot or one per subplot) per sampling occasion are recommended (see **Section 1.2. Number of trials and zonal split**). However, if local guidance is available this could be consulted when considering the number of replicates to take from the trial plots.

For untreated plots, at least two replicates should be taken for any control sampling event (typically at the beginning and end of the study but could spread throughout the trial). As with treated plots, the replicates may be taken from one large control plot or over multiple untreated subplots.

4. Field phase - Leaf sample processing and storage

4.1. Dislodging solution

A dislodging solution will be prepared (0.01% of Aerosol OT in water). An equivalent aqueous surfactant solution can be used if Aerosol OT interferes with the analytical procedure. It is recommended to use the same supply of water to prepare the dislodging solutions for all trials in a study (even if conducted in several countries) and for all analytical work requiring blank dislodging solution (i.e., matrix based standard solutions, procedural recoveries, ...) to exclude matrix-based effects during further data processing. Its preparation will be documented in the raw data.

4.2. Leaf sample processing

The dislodging procedure consists of mechanically shaking leaf material samples in a dislodging solution, and standardisation of this process within the trials of one study is encouraged, although Bruce et al.² have shown, that mainly shaking duration and identical number of dislodging repetitions (at least 2) between trials are amongst the key parameters of dislodging efficiency.

Therefore, parameters worth considering in the dislodging process include: duration, the dislodging solution volume, the dislodging container geometry (round vs. squared) and size, and the physical shaking parameters during orbital shaking, namely the orbital radius of the shaker and the angular velocity, which is a function of the selected RPM (revolutions per minute). In a study with several trial sites, it is highly likely, that different shakers with different fixed orbital radii are being used, whereas the other influencing parameters may be harmonised procedurally (same dislodging volume, same dislodging time, number of repeated dislodging cycles, container geometry). Therefore, it is recommended to adopt the angular velocity of different shakers

² Bruce, E.; Korpalski, S.; Johnson, D.; Klöner, D.; Nagel, W.; Holden, L.; Lange, B. Effect of dislodging techniques on foliar residue determination for agricultural crops Arch. Environ. Contamin. Toxicol. 50, 138-143 (2006) Doi: 10.1007/s00244-005-7041-6

used within one study to account for different physical shaker differences as described in Appendix B - DFR dislodging procedure via orbital shaker. All other mentioned parameters should be consistent for all trials and sampling occasions in a given study.

A typical procedure for a 400 cm² leaf disc sample is as follows:

100 mL of dislodging solution will be poured into the jar containing the leaf material sample (no previous sample transfer into another container). All containers from one sampling occasion will be installed on an orbital shaker and the angular velocity (RPM) will be selected based on the shaker orbital radius. The shaker will then be operated at the selected angular speed for a selected duration (typically 10 min). The dislodging solution will be decanted into a separate suitably sized container. Another 100 mL of dislodging solution will be added to the leaf discs remaining in the initial container and the shaking procedure will be repeated. The second lot of dislodging solution will be decanted into the same container as the first 100 mL lot of dislodging solution to generate a composite 200 mL sample. At this point in time the opportunity exists to verify that the correct number of discs has been sampled prior to discarding the leaf discs.

This final container with the 200 mL dislodging solution will be securely capped before thorough mixing by manual shaking. Subsequently, aliquots for residue analysis can be subsampled. Consideration should also be given to the option for “ship” and “retain” samples as back-ups for potential shipping issues, with retain samples remaining at the field station unless required.

For “entire leaf” sampling – the leaf wash approach requires adaption of the dislodging solution volume to maintain 2 x 100 mL/400 cm² of foliage. Depending on the selected container size and container geometry for entire leaf material sampling and the derived leaf surface area of the entire leaves, a dislodging solution volume corresponding to the 2 x 100 mL/400 cm² ratio should be selected for this approach. The container size and the volume must be sufficiently large to allow adequate agitation to ensure residue removal from whole leaves is analogous to leaf disc washing procedures.

Leaf dislodging solution samples shall be transferred to a freezer (-18°C) after completion of the dislodging process.

When control leaf samples will be collected, they will be submitted to the same dislodging procedure as the treated leaf samples.

In the case that leaf material samples are dislodged at a site remote from the field trial location, the leaf material samples should be transported to this site under cool conditions using blue ice or equivalent. Leaf material shall not be frozen between sampling and dislodging.

Dislodging of the leaf material samples should start within 4 hours of sampling completion.

4.3. Leaf sampling containers and storage conditions

The design of DFR sampling, dislodging and storage procedures may require specific adaptation to account for properties of the analyte (see also **Section 5.2. Fortification solutions**). E.g., the sampling and dislodging containers may need to be made of glass instead of plastic material to avoid/limit surface adherence. The addition of appropriate keepers (buffer, organic solvent etc.) may be considered to ensure analyte stability

or avoid surface interaction during sampling and/or storage. The appropriate storage container should be kept away from light to avoid photolytic degradation of samples.

Ideally these compound specific properties should be established during the analytical method development step prior to the field study conduct.

4.4. Identification, handling, storage and shipment of DFR solution containers

Samples should be uniquely identified. Each container sample will be labelled and introduced in a labelled plastic bag after checking the two labels match.

DFR samples and field fortification samples will be stored in containers of identical material (see **Section 5.2. Fortification solutions**).

Samples will be stored frozen ($\leq -18^{\circ}\text{C}$) immediately after completion of the dislodging procedure and ≤ 2 hours after start of dislodging procedure. Care will be taken to place and keep the containers upright at least until the solutions are frozen.

4.5. Solid Phase Cartridge (SPE) approach

The Solid Phase Extraction (SPE) based approach for DFR studies streamlines field sampling, preserves analyte stability, and may simplify sample shipping. Immediately after foliage dislodging procedure is completed, a defined amount of a stable isotopically labelled internal standard is added to the solution to allow analytically accurate quantification across all samples.

A small aliquot of each dislodging solution is loaded directly onto preconditioned SPE cartridges in the field. Once loaded, the cartridges are sealed in labelled zipper bags and frozen, where the pesticide residues remain stable and securely retained on the sorbent. This eliminates the need to ship frozen liquid extracts - avoiding common issues such as broken bottles, leakage, and degradation during transit. Further details on the SPE methodology can be found in US EPA Method 3535A.

5. Field phase - Field fortification

5.1. Control wash solution preparation for field fortification experiments

The required amount of leaf samples for control wash solution preparation will be taken from the control plot on each day when field fortifications are scheduled. The amount of leaf material collected must meet the requirements to perform the fortification experiments at the scheduled fortifications levels with the target number of replicates including control samples.

5.2. Fortification solutions

To ensure accurate reproducibility of the fortification process it is preferable to use a reference item prepared in solvent where homogeneity and stability can be checked by the analytical laboratory before being dispatched to the field site.

Whilst the formulated test item could be used, preparation of homogeneous low-level fortifications can be more challenging to ensure the correct dose is achieved.

Field fortification samples should be provided for all analytes tested, to verify analyte storage stability.

It is recommended that analytical method development should be conducted before any field trial in order to determine appropriate parameters and conditions for field sample generation and storage until analysis (see **Sections 3 and 4**). This preliminary step could include tests for the container material used for leaf processing and for storage of the resulting wash solution samples (and fortification samples). If there are corresponding stability instructions for a product/test item, e.g., with regard to photosensitivity, hydrolytic stability, etc., these should be mapped accordingly in the study protocol and considered in the method validation. If there is a risk of analyte adsorption to the chosen container lid (which may be made of a different material), special care will be taken to keep the sample containers upright. Field and analytical Principal Investigators shall agree to use the same material for those containers before any field work starts, as well as agreeing on the type of equipment to use for the fortification procedure (micro pipette, glass pipette, Hamilton syringe, etc.). In addition, method validation should preferably also address potential leaf matrix effects and fortification solution stability in the chosen solvent at the foreseen shipping and storage temperature.

The field fortification solutions will be prepared at the analytical laboratory prior to the start of the trial, using the analytical reference item of analyte of interest diluted in an appropriate solvent. The stability of the field fortification solutions should be checked to ensure solutions can be stored for the expected period of time prior to their use in the fortification experiments. Appropriate storage conditions should be maintained for field fortification samples throughout the trial period including shipment to and from the test site. A temperature data logger could remain with the solutions from preparation until the end of their use (and eventually until return to the analytical test site).

5.3. Number of field fortifications

At least one series of field fortifications has to be conducted per trial. In case only one field fortification experiment is scheduled, this should be conducted on the day of the first application to cover the entire storage period. In this case, interim DFR specimen shipments to the analytical laboratory are not possible due to the fact that only one set of field fortification samples is available to cover storage and shipment of the entire DFR samples collected in that trial. Further fortification experiments may be conducted during the trial period, preferably on the days of applications, and during the decline sampling period following the last application. A last series of field fortifications could be conducted on the last day of sampling (see **Section 4. Field Phase - Leaf sample processing and storage**) for details on the levels to be targeted in that situation).

A field fortification experiment should consist of at least 2 control (blank) samples, 3 low level fortifications and 3 high level fortifications. In the case of expected rapid decline of the analyte in the dislodging solution an additional fortification level should be added to the field fortification experiment. Typically, fortification solution concentrations should not exceed a factor of 100, therefore proposed fortification solution concentrations could be 10xLOQ, 1,000xLOQ, and 100,000xLOQ, always considering, that the fortification levels should bracket the expected analyte concentrations in the dislodging solutions.

Additional series of field fortifications could be conducted if variable environmental conditions are expected during processing and/or storage along a trial. For example, if several sample shipments to the analytical test site have to be organised due to limited stability of the analyte in samples, one series of field fortifications must be included per shipment. Typically, the series of field fortifications included in a shipment will cover the longest storage period of the DFR samples shipped.

5.4. Levels of field fortifications

The low and high fortification levels should bracket the range of the anticipated levels of analyte in DFR samples during the trial.

5.5. Spiking of the control wash solutions

Depending on the preliminary analytical work and preparation of the fortification solutions, the method for spiking a control wash solution could be one of the following methods, however this is not a restrictive list:

- Spiking using a pipette procedure i.e., usually a micro pipette (but if test item requires alternatives e.g., using glass pipette, Hamilton syringe maybe applied) to deliver a volume measured by a field team member from a vial containing a sufficient volume for several fortification samples, or
- Prepare a container/vial (e.g., container volume of 10 mL) with fortified solution in the analytical test site that already contains the required amount of reference item, e.g., the formulation / active substance / isomers / metabolites; it can already contain internal standard. Then add a defined quantity of the sample wash solution (aliquot) (e.g., 5 mL) to this container, or
- Emptying the content of a vial prepared at the analytical test site (each vial + lid will be weighed before and after emptying) in a defined quantity of wash solution, or
- Emptying the content of a vial prepared at the analytical test site and dropping the vial + lid into the fortified solution (the label on the vial should be carefully removed beforehand).

Possible addition of keeper (see **Section 4. Field Phase - Leaf sample processing and storage**), packaging, storage and shipment of the field fortification samples will be the same as for the DFR samples.

Control wash solutions will be fortified at ambient temperature after sampling before the sample is frozen. The fortification solutions will also be used when at ambient temperature. It needs to be ensured that after unfreezing the fortification solutions are homogeneous if in a suspension form.

5.6. Identification, handling, storage and shipment of samples

It needs to be ensured that the labels adhere properly to the container and the bag even under frozen storage conditions.

The material of the jars used to store DFR samples and field fortification samples should be the same.

Samples should be stored frozen ($\leq -18^{\circ}\text{C}$) immediately after fortification of the leaf wash and ≤ 2 hours after start of dislodging procedure. Special care should be applied to place and keep the containers upright at least until the solutions are frozen.

Samples (and remaining fortification solutions if scheduled to be sent back to the laboratory) should be sent under deep frozen conditions to the analytical Test Site.

Dislodged leaves should be disposed of safely as contaminated waste.

5.7. Analysis of field fortification samples

Field fortification samples shall be analysed along with the DFR samples, either in the same analytical series or on consecutive days. The period of storage of field fortification samples should always be equal to or longer than the period of storage of the DFR samples to ensure the period of storage of DFR samples is fully covered.

6. Data reporting and adjustment for recoveries

6.1. Residue data presentation in a study report

All residue data shall be presented.

Correction for background residues should not be performed.

Measured, uncorrected (μg active substance per mL) and converted values into $\mu\text{g}/\text{cm}^2$ (or mg/cm^2) per leaf surface area are reported. Dislodged leaf surface area per sample should be reported, ensuring both sides of the leaf are considered (i.e., area of double-sided leaf disk).

All field recovery results should be reported and the corresponding correction approach applied to the measured DFR samples should be reported.

If a DFR is below the limit of quantification (LOQ) and above the limit of detection (LOD), this should be reported as below LOQ (presented e.g., <LOQ).

If a DFR is below the limit of detection (LOD), this should be reported as below LOD (presented e.g., n.d. or <LOD).

A DFR reported as <LOQ or <LOD (or n.d.) is replaced by the LOQ or the LOD value, respectively, in further calculations.

DFR values normalised for application rate could be reported (in $\mu\text{g}/\text{cm}^2/\text{kg as}/\text{ha}$ units).

6.2. Exclusion of an outlier residue

A holistic view on all available DFR data of the study is required and expert judgement applied to determine any technical or statistical grounds for excluding any potential outlier.

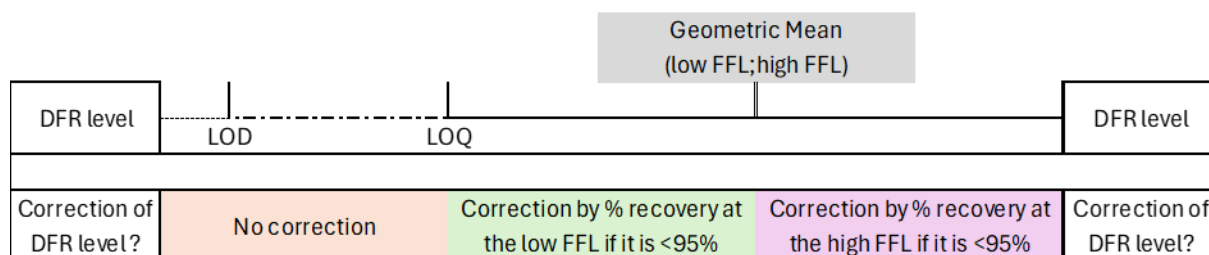
6.3. Consideration of recoveries

6.3.1. Correction by field recoveries

A DFR which is <LOQ or <LOD is not corrected whatever the field recovery data shows.

Adjustment of a measured DFR with corresponding field recoveries is usually and **arbitrarily** done when field recoveries are <95% and no correction of a measured DFR is done when the corresponding field recoveries are ≥95% (approach adopted by EFSA). This is a valid approach. Other thresholds for adjustment could be considered according to expert judgement.

For a measured DFR between two field fortification levels, correction is done with the nearest recovery value on either side of the geometric mean of the two fortification levels.



FFL = Field fortification level

LOD = limit of determination

LOQ = limit of quantification

If several series of similar field recoveries are generated during one trial, all recoveries should be pooled per fortification level over all series, to result in one mean recovery percentage per fortification level for the full trial. However, expert judgement should be taken when the above approach is deemed not scientifically appropriate.

Low field recoveries are not a measure of study quality, therefore a lower limit (e.g., <70%) for field recoveries used for correcting measured values cannot be set. It may be impacted by, e.g., a.s. properties, environmental/storage conditions, and matrix properties, etc.

6.3.2. Laboratory (procedural) recoveries

During the analytical phase at the laboratory after the field phase, procedural recoveries are done to assess the analytical performance of the method in terms of accuracy and repeatability for each analytical set (including field fortification samples and/or DFR samples). These procedural fortifications are freshly prepared at the analytical facility by fortification of control wash solution with the analyte under investigation and the subsequent determination of the analyte recoveries applying the analytical method.

Depending on the active substance concentration in procedural recovery experiments an analyte recovery range from 60-70% to 110-120% is considered to confirm analytical method validity according to SANTE/2020/12830, Rev.2 (14 Feb 2023). These limits apply only to procedural/concurrent/lab recoveries and not to field recoveries.

Correction of measured DFR samples for procedural recovery must not be performed on top of correction for field fortification as this correction would effectively double count laboratory losses (see **Appendix C** for more information).

7. DFR derivation

At each sampling timing, the appropriate DFR value should be derived. Depending on the number of replicate samples and sample timing, various approaches could be applied to derive a relevant DFR value.

7.1. Statistical approach

For derivation of average DFR values, the same statistical approach should be applied to both field plot (field trial) DFR and multiple trial DFR values. As DFR data is expected to follow a log-normal distribution the geometric mean values should be derived for both scenarios, however, it is acknowledged that historically arithmetic means have been applied to DFR data and they could be used instead.

7.1.1. DFR derivation per field plot and sampling timepoint

The DFR for a field plot at a given sampling timepoint is the geometric mean of the replicate DFR values determined when ≥ 3 replicates are taken from the field plot. The highest DFR is expected to be retained if less than three replicates are available but expert judgment should always be considered.

7.1.2. DFR derivation If multiple trials are available, e.g., sites, residue zones

The overall DFR for a study (or collection of trials) is the geometric mean of the DFR values determined for each relevant trial per timepoint when ≥ 3 trials are included in the dataset (i.e., study geomean of trial geomeans), see schematic table below.

		DFR_0DAA1	DFR_0DAA1	DFR_0DAA1
		Replicate DFR	Trial DFR	Study DFR
Study 1	Trial 1	Replicate 1	Geomean (of replicates)	Geomean (of trial-geomeans)
		Replicate 2		
		Replicate 3		
	Trial 2	Replicate 1	Geomean (of replicates)	
		Replicate 2		
		Replicate 3		
	Trial 3	Replicate 1	Geomean (of replicates)	
		Replicate 2		
		Replicate 3		

7.1.3. DFR derivation If two trials are available, e.g., sites, residue zones

The higher DFR geomean of the two trials is expected to be retained if less than three relevant trials are available but expert judgment should always be considered.

		DFR_0DAA1	DFR_0DAA1	DFR_0DAA1
		Replicate DFR	Trial DFR	Study DFR
Study 1	Trial 1	Replicate 1	Geomean (of replicates)	Highest of the two trial geomeans
		Replicate 2		
		Replicate 3		
	Trial 2	Replicate 1	Geomean (of replicates)	
		Replicate 2		
		Replicate 3		

7.2. Definitions of default DFR (DFR_{DEF}), DFR₀, DFR_X and DFR_{NORM}

7.2.1. Default DFR (DFR_{DEF})

Default DFR (DFR_{DEF}): The EFSA default DFR value of 3 µg/cm²/kg a.s./ha is an example of a normalised DFR value. This value assumes a DFR of 3 µg/cm² if 1 kg a.s. is applied per hectare. This DFR_{DEF} can therefore be combined with different application rates to predict DFR values. For example:

- An application at 0.5 kg a.s./ha would result in a DFR equal to 1.5 µg/cm².
- An application at 2 kg a.s./ha would result in a DFR equal to 6 µg/cm².

DFR₀: The DFR₀ according to EFSA guidance³ is defined as the residue level determined at the earliest feasible timepoint after application (after spray has dried) and expected to reflect the highest residue level before residue decline is becoming effective. However, this definition is not specific enough for deriving relevant DFR values for exposure assessment, therefore multiple time-dependent DFR definitions (DFR_X) are suggested instead and DFR₀ should no longer be used.

7.2.2. GAP specific DFR (DFR_X)

DFR_X: As the DFR after a single product application may be lower than the DFR₀ after multiple applications (compare e.g., below DFR_0DAA1 versus DFR_0DAA2) due to potential accumulation, we suggest specifying the application number when presenting the data, e.g.,

- DFR_0DAA1: DFR 0 Days After Application 1
- DFR_0DBA2: DFR 0 Days Before Application 2
- DFR_0DAA2: DFR 0 Days After Application 2
- DFR_2HAA2: DFR 2 Hours After Application 2

³ EFSA, 2022: Charistou A., Coja T., Craig P., Hamey P., Martin S., Sanvido O., Chiusolo A., Colas M. and Istace F., 2022: Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. <https://doi.org/10.2903/j.efsa.2022.7032>

- DFR_7DAA3: DFR 7 Days After Application 3

DFR_X values can be considered as GAP/scenario specific DFR values and will always be recorded in $\mu\text{g}/\text{cm}^2$. These measured (and not normalized) values are derived following a specific application regime (GAP) and are only relevant for use in risk assessment scenarios where the GAP is considered to be the same or reduced (i.e., is less worst-case, examples of which could include, lower application rates, lower number of applications, longer intervals between applications).

This approach can be followed with an expected overestimation of exposures for GAP rates lower than the GAP used to derive the DFR_X value because the amount applied to the plant will be less than that used to derive DFR_X.

However, it is not considered suitable to use the measured values as measured for assessment of higher GAPs. In turn, applicants will be obliged to use the conservative default DFR (DFR_{DEF}) value, which does not take into account the behaviour of the specific product.

To overcome this limitation, normalised DFR values (DFR_{NORM}) can be derived from the DFR data set and be used with any application rate to generate a product specific DFR estimation for any GAP.

7.2.3. Normalised DFR (DFR_{NORM})

Measured DFR_X values in $\mu\text{g}/\text{cm}^2$ can be normalised to a DFR_{NORM} in $\mu\text{g}/\text{cm}^2/\text{kg a.s.}/\text{ha}$ if the amount of DFR measured is known to come from a given application rate. DFR_{NORM} considers the residue level determined at the earliest feasible timepoint after application (after spray has dried). There are three scenarios/methods that can be used to derive a DFR_{NORM} (examples for all methods are provided in Appendix D -).

- The simplest and most common method to derive a DFR_{NORM} is to use the DFR_0DAA1 value and divide this by the application rate (in kg a.s./ha). In this case, all of the measured DFR will have resulted from a single application so no additional manipulation of the DFR value is required.
- If multiple applications are made to the same crop during its growing season, additional normalised DFR_{NORM} values can be calculated by subtraction of the pre-application DFR_X (e.g., DFR_0DBA2) value from the DFR_X taken immediately after the application (e.g., DFR_0DAA2). This method allows an estimation of DFR from a known application rate by effectively resetting the DFR to zero from previous applications and thus getting DFR as if after a single application. Note that for this approach, samples must be taken immediately before the application and immediately after the application (i.e., once the application has dried).
- For multiple applications, where the pre-application DFR_X is not available, a normalised DFR_{NORM} can still be derived if the DT_{50} is known. Using DT_{50} data one can estimate the amount of a.s. remaining on the leaf surface from previous applications, whilst also considering the dissipation of the active substance by applying a multiple application factor (MAF). Following this method

the normalised DFR_{NORM} can be derived by dividing the DFR_X by the MAF corrected application rate. A MAF adjusted application rate⁴ could be estimated as follows for a 3-application scenario:

$$DFR_{NORM} = DFR_{ODAA3} / \text{MAF adjusted 3 app rate}$$

$$\text{MAF adjusted 3 app rate} = ([Dose A1 * e^{(-k*t_1)}] + [Dose A2 * e^{(-k*t_2)}] + [Dose A3])$$

Where: $k = \ln(2)/DT_{50}$, t_1 = time interval between A1 and A3, and t_2 = time interval between A2 and A3.

If the GAP followed was 3 x 1 kg a.s./ha with 7-day interval and a DT_{50} of 10 days:

$$\text{MAF adjusted 3 app rate} = [1 \text{ kg a.s./ha} * e^{(-\ln(2)/10*14)}] + [1 \text{ kg a.s./ha} * e^{(-\ln(2)/10*7)}] + 1 \text{ kg a.s./ha} = 0.38 \text{ kg a.s./ha} + 0.62 \text{ kg a.s./ha} + 1.00 \text{ kg a.s./ha} = 2.0 \text{ kg a.s./ha}$$

So, for this example assuming $DFR_{ODAA3} = 2 \mu\text{g}/\text{cm}^2$ and MAF adjusted rate = 2 kg a.s./ha

$$DFR_{NORM} = 2 \mu\text{g}/\text{cm}^2 / 2 \text{ kg a.s./ha} = 1 \mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$$

Using one of the three normalisation approaches described above a geometric mean normalised DFR_{NORM} value can be derived for each trial based on the individual DFR_{NORM} values derived if ≥ 3 DFR_{NORM} replicates are available within a trial. If < 3 DFR_{NORM} replicates are available, the highest DFR_{NORM} can be used (as described above).

7.3. Using DFR values in risk assessment

When using DFR values in risk assessment the applicant has two options:

- Normalised DFR_{NORM} (in $\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$) can be used in a calculator/model which combines normalised DFR values with a MAF corrected application rate. With this approach a DT_{50} value must be included in the calculations to derive a MAF corrected application rate. The DT_{50} could be a default value or valued derived following the method set out in **Section 8. DT_{50} derivation.**
- Measured DFR_X values (in $\mu\text{g}/\text{cm}^2$) should be used outside of a calculator/model using the below formula to derive a GAP specific exposure estimation. In this case measured DT_{50} values are irrelevant as they are built into the DFR_X value.

$$\text{Exposure (mg a.s./kg bw/day)} = (DFR_X(\mu\text{g}/\text{cm}^2) \times TC(\text{cm}^2/\text{h}) \times T(\text{h}) \times DA) / (BW(\text{kg}) \times 1000)$$

Where TC = transfer coefficient, T = time, DA = dermal absorption, BW = body weight.

Risk assessments following either of these approaches are considered equally valid, the applicant should use expert judgment when choosing which approach to take for a given risk assessment.

⁴ EFSA, 2022: Charistou A., Coja T., Craig P., Hamey P., Martin S., Sanvido O., Chiusolo A., Colas M. and Istace F., 2022: Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. <https://doi.org/10.2903/j.efsa.2022.7032>

7.4. Use of measured DFR_X in modelling tools such as EFSA 2022 online tool

The use of a DFR_X value is not recommended in the EFSA online tool. The tool does not include an entry field for DFR_X values, instead the tool only allows normalised DFR values to be input into the tool. Whilst the inclusion of the DFR_X values can come out with the correct worker exposure for the given scenario covered by the DFR_X value (e.g., DFR_3DAA4) by artificially setting the application rate to 1 kg ai/ha, the report output will not be representative of the GAP for operators, residents and bystanders and may be difficult to interpret without thorough explanation.

8. DT₅₀ derivation

A kinetic evaluation to derive DFR DT₅₀ and DT₉₀ values should follow the standard recommendations of FOCUS kinetics (2014)⁵ and EFSA 2019 Technical Report⁶. However, where local guidance is available then local guidance should be followed.

Evaluations can be done using the latest available software package versions, e.g., KinGUI v2.1⁷ or CAKE v4.0⁸.

DFR DT₅₀ and DT₉₀ value derivation for modelling purpose should follow to the recommended workflow in **Section 8.4. Identification of the appropriate model**. It is worth highlighting that the following guidance is focused on the kinetic evaluation of applied substances (i.e., parent compounds), not on metabolites.

8.1. Number of data points

The leaf sampling schedule for a foliar DT₅₀ derivation is also discussed in **Sections 2 and 4**.

To determine dissipation rates of dislodgeable residues, ideally the data should be sufficient to cover a period as long as several half-lives (e.g., 3 x DT₅₀), which is consistent with other modelling guidelines, requiring either:

- Time-points when test substance DFR has reached <10% of initial value DFR_ODALA⁹.

⁵ FOCUS, 2014: Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. FOCUS Work Group on Degradation Kinetics, Version 1.1., 18 December 2014 [FOCUSkineticsvc1.1Dec2014.pdf](https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/sp.efsa.2019.EN-1673) ([europa.eu](https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/sp.efsa.2019.EN-1673))

⁶ EFSA, 2019. European Food Safety Authority, 2019. Technical report on the outcome of the Pesticides Peer Review Meeting on general recurring issues in ecotoxicology. EFSA Supporting publication 2019:EN-1673. 117 pp. <https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/sp.efsa.2019.EN-1673>

⁷ Meyer H. and Witt J., 2014: KinGUI v2.1 Manual for the Graphical User Interface. Bayer CropScience AG. KinGUI download: <http://kingui.vrbka.net/KinGUIv2.1.zip>

⁸ CAKE, 2026: CAKE - Computer Assisted Kinetic Evaluation, v. 4.0. Developed by the Applied Computational Sciences team of Capgemini Engineering (formerly Tessella), sponsored by Syngenta Ltd.. CAKE download: <https://cake-kinetics.org/>

⁹ EFSA, 2014. European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662, 37 pp. <https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2014.3662>

- Sampling until the DT_{90} has been reached⁵.

At least five quantifiable timepoints should be available for fitting the decline curve, after the elimination of outliers, non-detects or a lag phase⁵. However, in some exceptional cases, four points may be enough (e.g., fast dissipation of the active substance, until residues < LOQ), but the points should never be fewer than four.

The number of time points must be (appreciably) larger than the number of parameters fitted, i.e., (number of time points) at least for: $SFO \geq 4$, $FOMC \geq 4$, $DFOP \geq 5$, $HS \geq 5$.

However, if a sampling period does not cover the length of 3 half-lives, an appropriate kinetic evaluation and DT_{50} determination may still be possible in cases where enough data points are available to achieve a robust data fit.

8.2. Data-pre-processing

All measured replicates per timepoint within a field plot should be considered singularly, rather than using averages when deriving DT_{50} values. All experimental data sets and all single data points should be weighted equally (i.e., weighting factor 1). Adjustments for weighting suggested in the flow diagram in **Section 8.4. Identification of the appropriate model** should be ignored.

Values < LOQ, LOD: Residues below the limit of quantification (LOQ) or limit of detection (LOD) should be considered as follows:

- Values between LOD and LOQ should be set to the actual measured values, as given in the study report; if not provided they should be set to half the LOQ or LOD.
- All samples <LOD are set to half LOD.
- The curve should be cut off after the pesticide has largely dissipated. All samples after the first non-detect (<LOD) should be omitted unless positive detections above LOQ are made later in the experiment. In that case, samples are included up to the first non-detect (<LOD) which is NOT followed by later positive samples above LOQ.

8.3. Multiple applications

In case of multiple applications in one trial, multiple DT_{50} values may be derived if DFR data is available between the separate applications and considered as separate DT_{50} values. However, sufficient data points are typically only available after the last application. If several DT_{50} values can be evaluated for multiple applications, the geomean of all reliable values should be considered as the representative for the multiple application trial.

8.4. Identification of the appropriate model

This section and the flow diagram included at the end of it provides a process to identify the most appropriate kinetic model for a given data set.

For standard data entry:

- Time zero should be the initial residue values taken after the last application (DFR_ODALA)
- Use all available residue data, including single replicates.
- No weighting should be applied to residue data and no outliers should be omitted.

Processes like volatilisation, wash-off, photolysis, uptake, dilution due to plant growth, etc. usually form an initial rapid decline, followed by a slower dissipation. However, as the multiple application factor (MAF) is implicitly based on an SFO decay, it is recommended that SFO should be the default kinetic model applied to DFR data.

- **Step 1: Run SFO**
 - **SFO should be preferred**, if fit is acceptable.
 - SFO is acceptable if:
 - Chi^2 (X^2) error < 15 % (lab), < 25 % (field)¹⁰.
 - Residual plots should be randomly scattered. No systematic deviation should occur until the time when <10% of initial residues has been reached.
 - To improve the fit clear outliers may be removed.
 - It is not recommended to constrain the M_0 or apply weighting:
 - Constraining M_0 is not recommended for DFR decline data as initial foliar deposition is empirically variable and cannot be fixed to a defined reference point.
 - Weighting has not historically been applied to DFR decline datasets and no standardised approach exists for its implementation in this context.
- **Step 2: If SFO is not acceptable, run bi-phasic models**
 - **FOMC** (first order multiple compartment): if < 10% of initially measured residues remain by the end of the study acceptable if:
 - Chi^2 error < 15 % (lab), < 25 % (field)¹⁰
 - Residual plots should be randomly scattered. No systematic deviation should occur.
 - Use $\text{DT}_{50 \text{ pseudo SFO}} = \text{DT}_{90 \text{ FOMC}} / 3.32$.
 - **DFOP** (double first order in parallel) (1st choice) or **HS** (hockey stick): if > 10% of initially measured residues remain by the end of the study, acceptable if:
 - Chi^2 error < 15 % (lab), < 25 % (field)¹⁰, and
 - Residual plots should be randomly scattered. No systematic deviation should occur.
 - Use $\text{DT}_{50 \text{ slow phase}}$ (of k_2): where $\text{DT}_{50 \text{ slow phase}} = \ln(2) / k_2$
 - Expert judgement: If the slow phase represents just a small portion of the totally dissipating amount (e.g., g of DFOP > 0.75), then use $\text{DT}_{50 \text{ pseudo SFO}} = \text{DT}_{90 \text{ biphasic}} / 3.32$, or go back to FOMC.

If none of the bi-phasic models lead to a significantly improved fit, the SFO model might be chosen, if it is visually acceptable. The purpose of this rule is to avoid an over-parameterised model based on a marginally

¹⁰ 25% is a guide and is not a cut-off threshold; acceptability should be decided on a case-by-case basis.

better fit only. In general, the simplest model which describes the dissipation curve sufficiently well, should be preferred. The simplicity of a model can be easily defined by the number of free parameters (usually: SFO: 2; FOMC: 3; DFOP, HS: 4). The geomean DT_{50} of several studies should be used for further assessments.

It is worth noting that Chi^2 errors >25% is not an absolute value to reject a fit, however the model with lowest Chi^2 error is often the best fit.

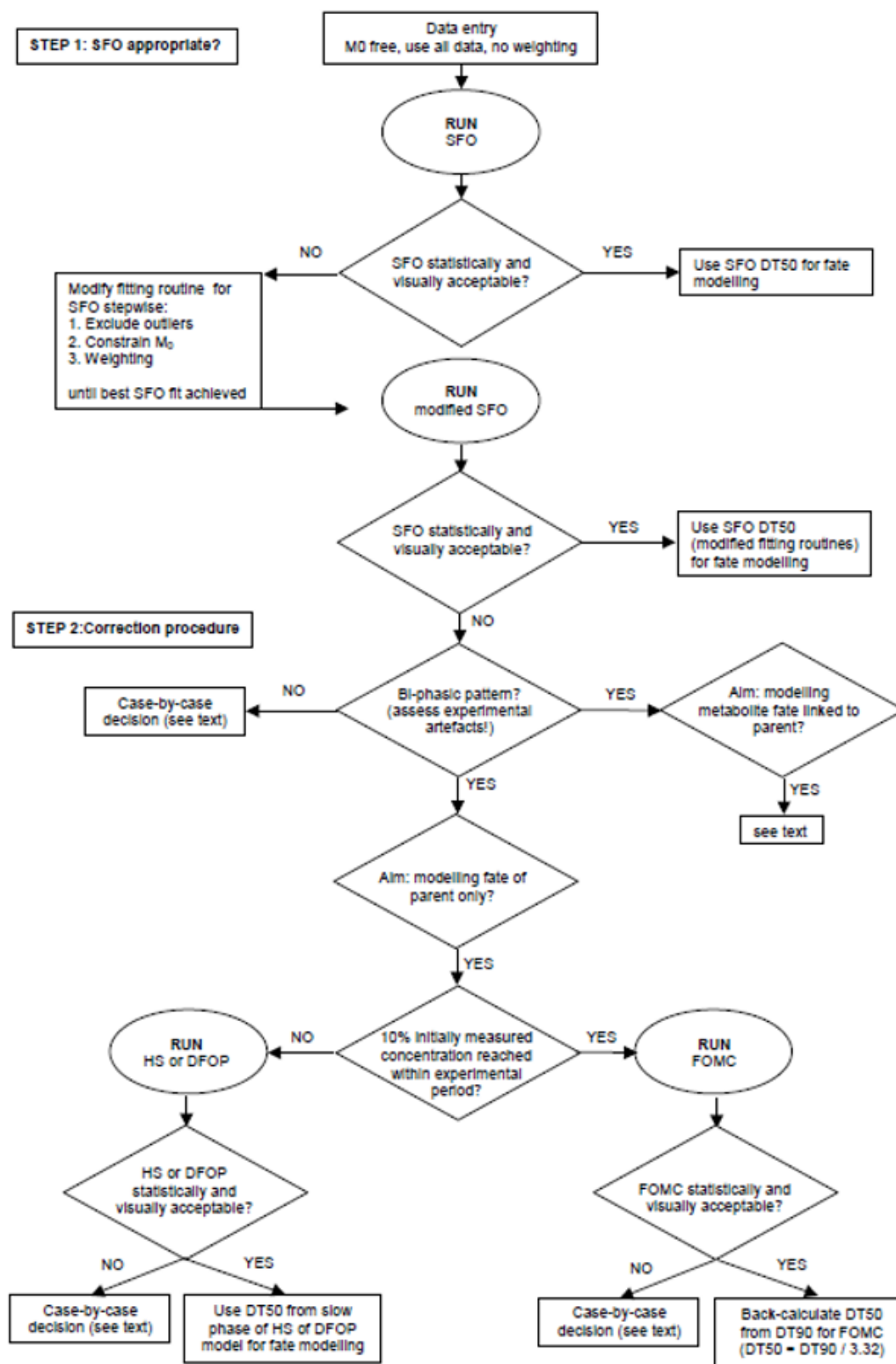


Figure 7-2. Recommended tier 1 procedure to derive degradation parameters for modelling the fate of a parent compound from degradation kinetics without a lag phase

(Taken from FOCUS, 2014, Section 7.1.2.1, page 117)¹¹

8.5. Weather conditions

In general, field residue trials are subject to local weather conditions (rain, humidity, temperature, wind, etc.). Daily rainfall, temperature and relative humidity data, should be reported for the evaluated residue trials. The location of a weather station and its distance from the trial site should be reported, ideally measurements should be taken no more than 1 km from the field. However, if this is not possible, data from weather stations <20 km distance from the experimental field may be used.

In some cases, rainfall may play a role, which should be carefully evaluated when assessing a dissipation trial. Rain events and their intensity could be plotted together with results of the residue quantification over time in order to identify sudden drops in the measured residue concentrations coinciding with such events. The kinetic assessment should also consider whether such episodes have a determinant role in the dissipation of the substance. It is worth noting that irrigation (e.g., sprinkler irrigation) should not be performed in DFR studies, as this could artificially increase the rate of dissipation.

There should be no rainfall for 24 h before and after an application. If the precipitation during the sampling period is higher than the typical precipitation at the field location, the study may not be acceptable for the estimation of DT₅₀. However, this should be decided on the basis of the resulting dissipation kinetics.

In some trials, it may be possible to reduce the impact of precipitation, by excluding sampling points which are strongly influenced by precipitation, e.g., at the beginning or end of study. If a sufficiently high number of sampling points is still available after deletion, these data can be considered appropriate for an evaluation.

In general, data of the best available physical weather station as close as possible to the trial location should be searched and its source reported, e.g., local station at trial site, publicly available data from official weather services.

As a last alternative, precipitation and temperature data from the appropriate MARS grid of the trial station (25 x 25 km grid width) and corresponding trial year can be used MARS, 2014¹². The European MARS database gives the following description for its rainfall evaluation in a 25 x 25 km grid:

“Parameter interpolation is executed in 2 steps: [...] As an exception, rainfall data are taken directly from the most suitable station.”

“Interpolated rainfall should be realistic in terms of number of rainy days, amount of rainfall and temporal distribution. The effects on the soil water balance and consequently on crop growth simulation of various small daily showers is different, than for example one large rainfall event per week. When rainfall data from several surrounding stations are averaged, the rainfall peaks are levelled off and the number of rainy days

¹¹ FOCUS, 2014: Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. FOCUS Work Group on Degradation Kinetics, Version 1.1., 18 December 2014 [FOCUSkineticsvc1.1Dec2014.pdf](http://efsa.europa.eu/EFSA_PDF/Focus/FocusKineticsvc1.1Dec2014.pdf) (europa.eu)

¹² MARS (2014): Interpolated meteorological data, JRC MARS Database. European Commission, Joint Research Center (JRC), MARS-AGRI4Cast, Ispra. <http://agri4cast.jrc.ec.europa.eu/DataPortal/Index.aspx?o=d>.

increases. Therefore, the CGMS takes for each climatic grid cell the rainfall of the most similar station i.e., the weather station with the lowest score for the concerned grid cell that has data. Only stations that satisfy the temporal availability check are included in the selection.”

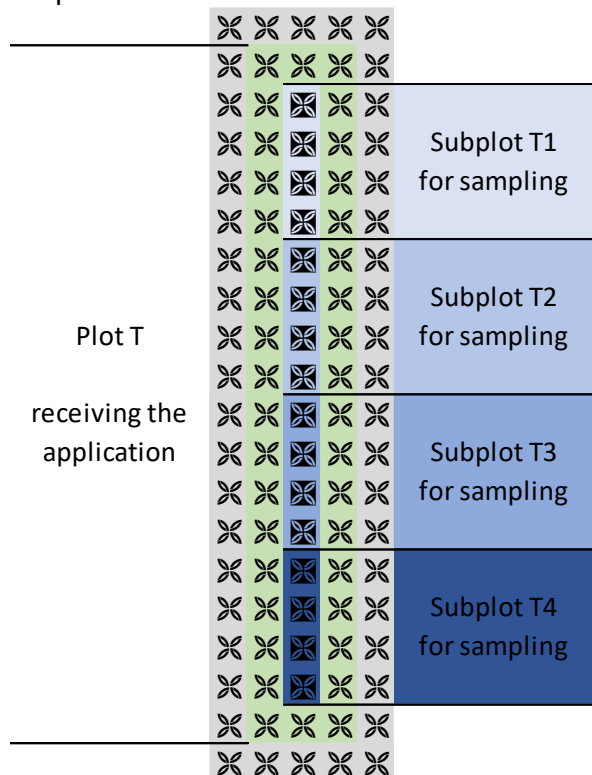
Based on these selection conditions, the precipitation amounts from the corresponding MARS grids are considered reasonably good to compare for the fallen rain amount in experimental residue trials.

In addition, it has to be noted, that often it is not known, if the precipitation at a sampling day did occur before or after sampling. Thus, the interpretation especially of significant rain amounts at sampling days are afflicted with a high uncertainty.

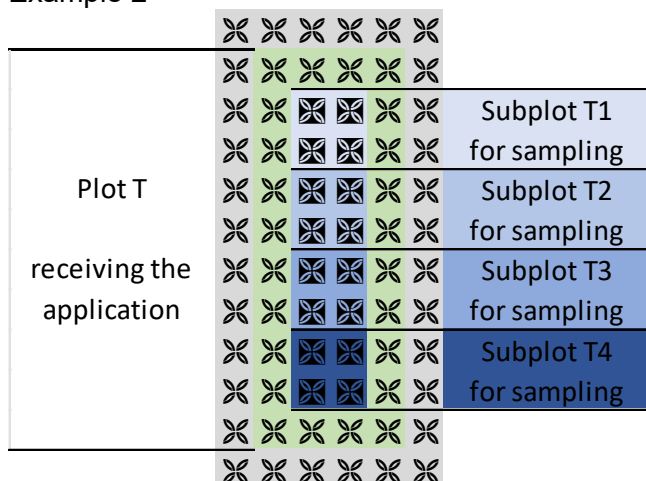
9. Appendices

Appendix A - Examples of plot designs for subplots and sampling

Example 1



Example 2



Example 3

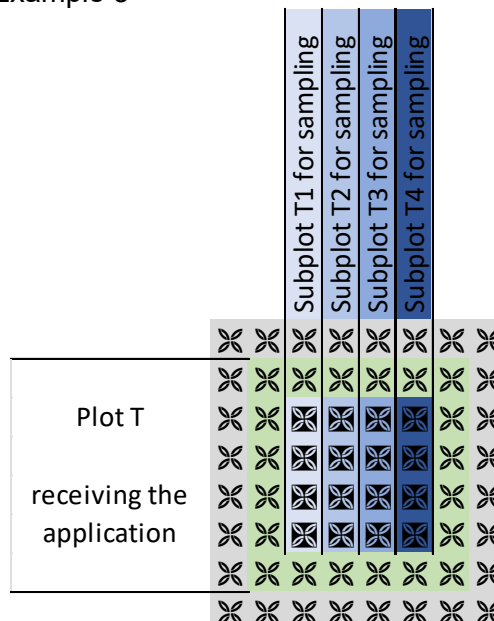
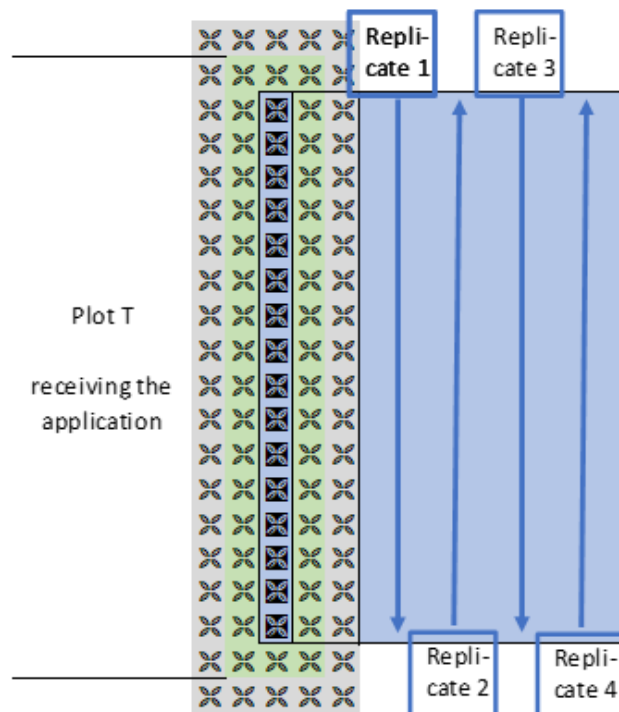


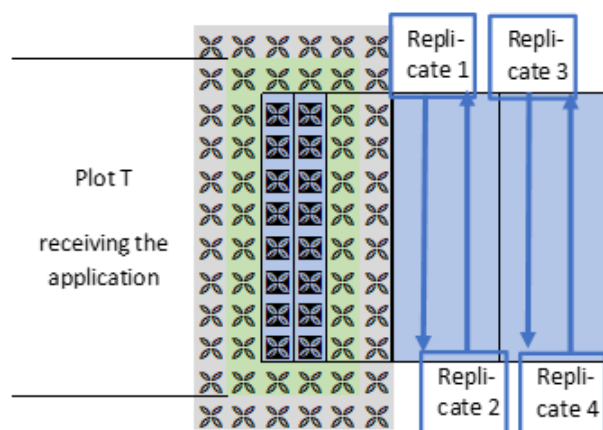
Figure 3 - Subplot approach: Examples of plot designs for individual plants/trees

	trees / vines / bushes / plants fully treated for taking samples
	trees / vines / bushes / plants fully treated but not for sampling
	trees / vines / bushes / plants not treated and not to be sampled, just for buffer

Example 1



Example 2



Example 3

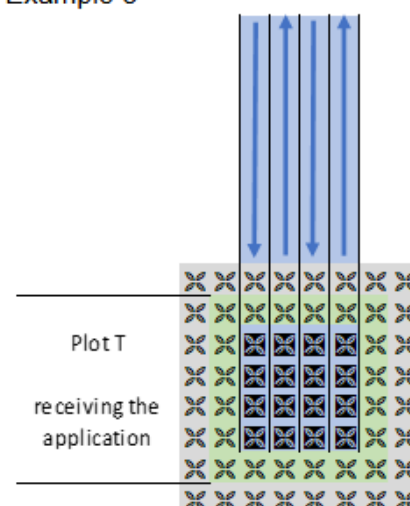
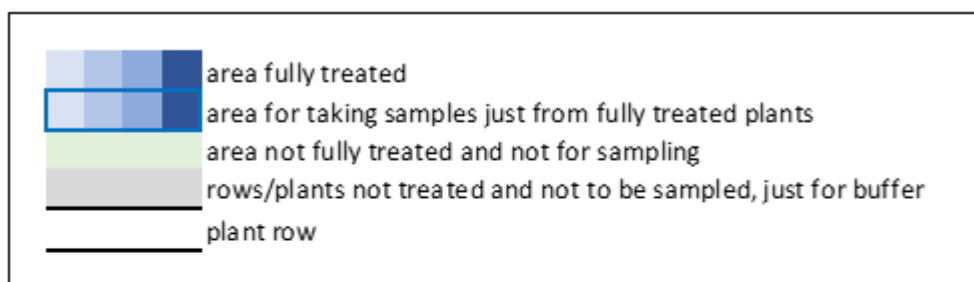


Figure 4: Repeated replicate approach: Examples of plot designs in total plot for individual plants/trees

For row crops, plots should be of sufficient size to allow collection of all necessary plant material without sampling the same plants twice or sampling border rows or plot ends, but not smaller than 100 m² (for a plot).

Examples of plot design for row crops like many vegetables, corn, beets and potatoes, applied with horizontal spraying equipment are illustrated in:

- Figure 5 (one example) for row crops under the subplot approach, and
- Figure 6 (one example) for row crops under the repeated replicate approach.



Example 1

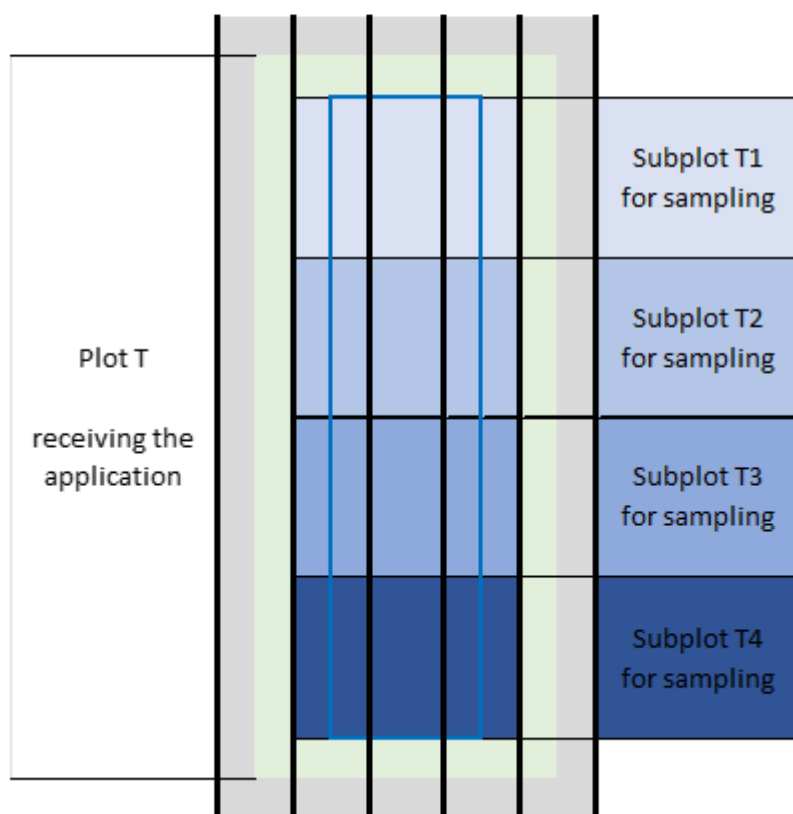
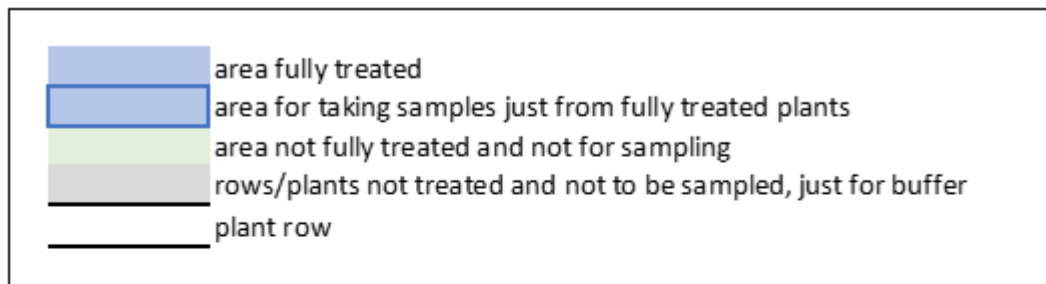


Figure 5: Subplot approach: Example of plot designs for row crops



Example 1

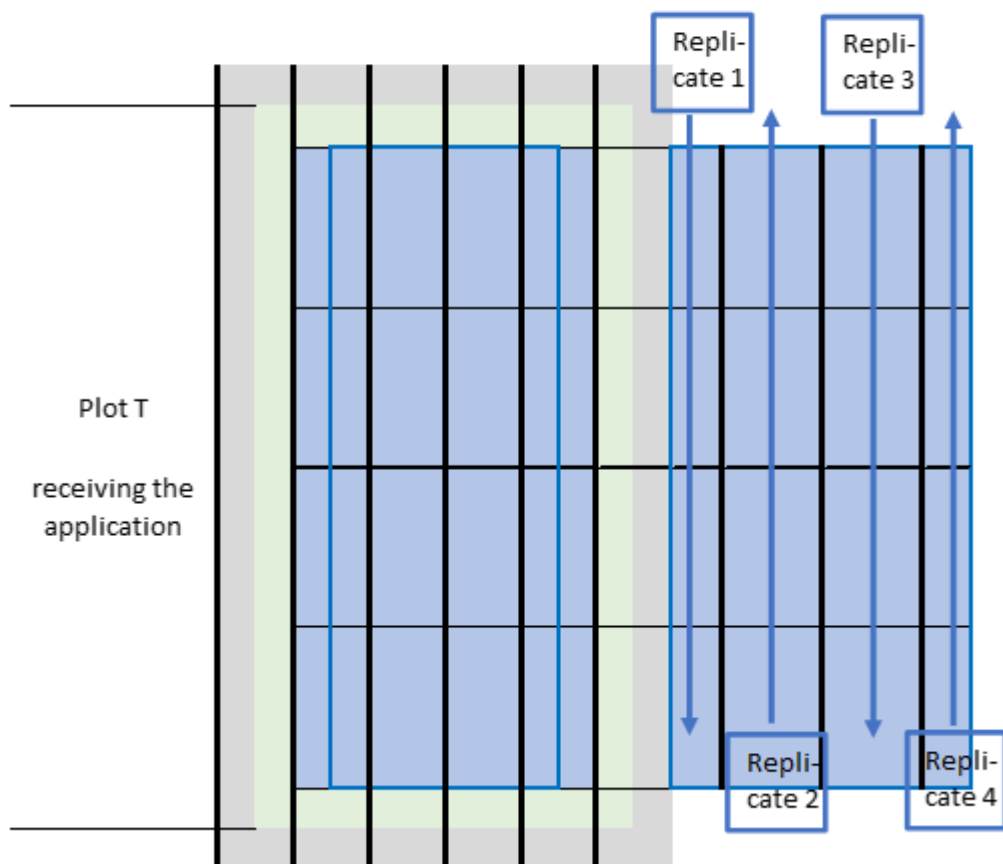
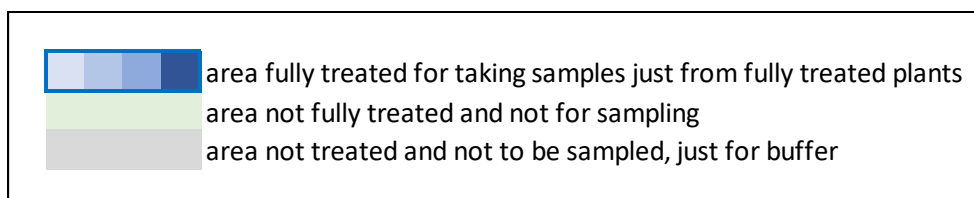


Figure 6 : Repeated replicate approach: Example of plot designs in total plot for row crops

For broad acre crops, a minimum size/sampling area is defined depending on the number of sampling events, as for row crops.

Examples of plot design for broad acre crops like cereals, applied with horizontal spraying equipment are illustrated in:

- Figure 7 (one example) for broad acre crops under the subplot approach, and
- Figure 8 (one example) for broad acre crops under the repeated replicate approach.



Example 1

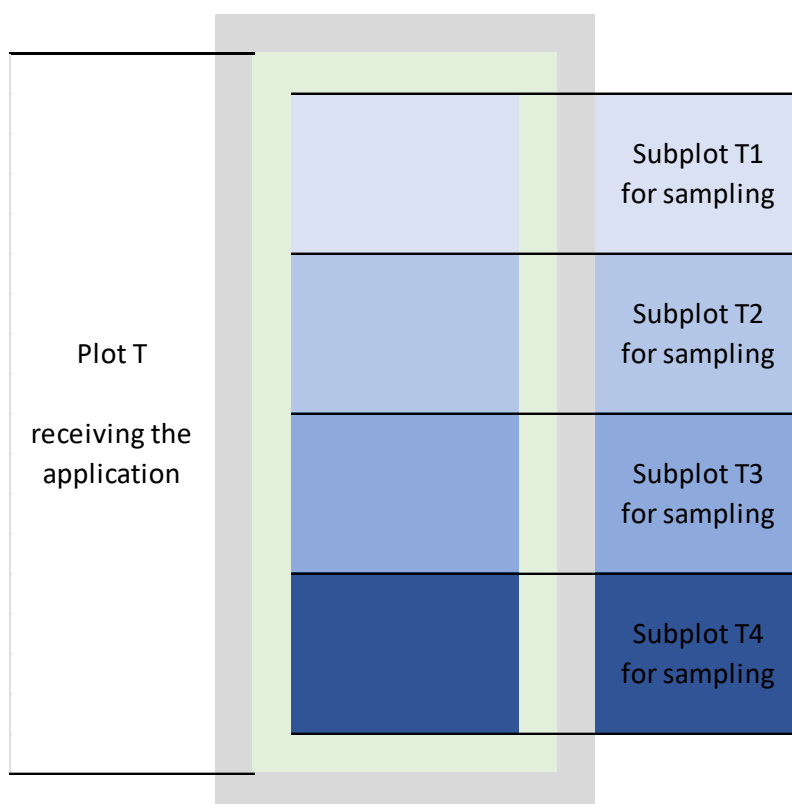


Figure 7: Subplot approach: Example of plot designs for broad acre crops

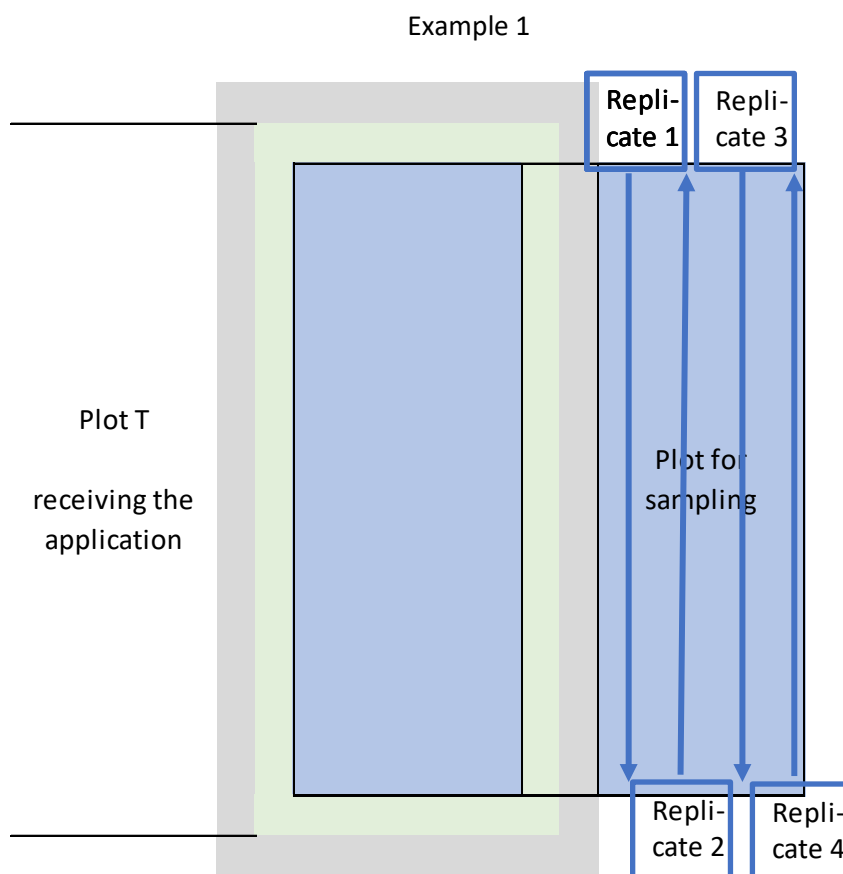
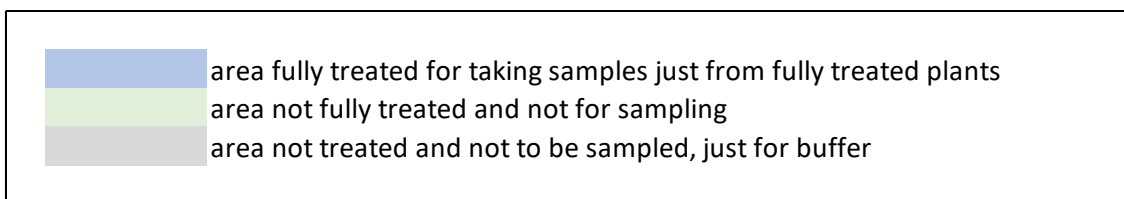


Figure 8: Repeated replicate approach: Example of plot designs in total plot for broad acre crops

A plot shall be large enough to allow spray application in a manner that reflects routine use (commercial practice more than experimental practice) and such that sufficient representative samples can be obtained without bias. Recommendations from the OECD Guideline for the Testing of Chemicals No. 509 – Crop Field Trial could be considered as a starting point.

A diagram is welcome in a study plan to visualize the expected layout, which may be different for row crops and tree crops.

Appendix B - DFR dislodging procedure via orbital shaker

Whereas dislodging parameters such as dislodging duration, the dislodging solution volume, the dislodging container geometry (round vs. squared) and size, and the number of dislodging cycles with new dislodging solution can be harmonised within the trials of one study, the orbital shaker types and consequently the orbital shaker parameters may be different between trials. Therefore, this annex provides guidance on how to how to potentially harmonise the shaking efficiency based on different physical shaker parameters.

Shaking Efficiency Considerations

Shaking Efficiency depends on:

- **Orbit radius:** Larger radius → more vigorous mixing.
- **RPM:** Higher RPM → faster mixing
- **Container shape and fill volume:** These influence fluid dynamics
- **Viscosity of the liquid (leaf surface area / dislodging volume):** More viscous liquids require more energy to mix.

The following figure is a diagram illustrating orbital shaking.

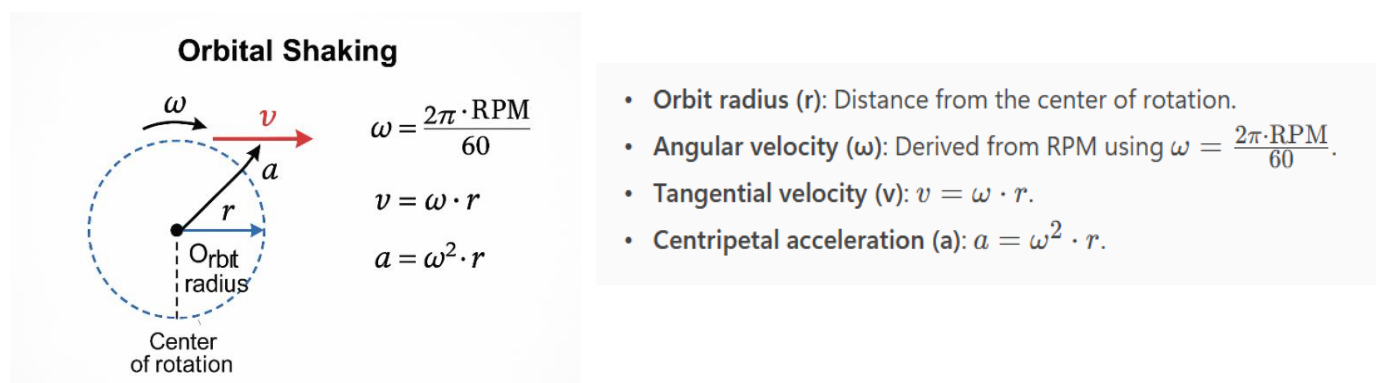


Figure 9: Orbital shaking parameters

Orbital (centripetal) acceleration is a valid and quantifiable measure of shaking efficiency. It can be used to compare the shaking performance of orbital shakers with different orbit radii, even if they operate at the same or different angular velocities.

Therefore, setting a target orbital (centripetal) acceleration for leaf material dislodging will enable the researcher to derive the appropriate RPM for his shaker with a fixed orbital radius.

The following are two examples how to derive the RPM values for two orbital shakers with different orbital radii to result in identical orbital acceleration and as such to provide comparable shaking efficiencies for valid DFR data generation.

Derivation of shaker RPM for given orbital acceleration

Objective

To determine the required rotational speed (RPM) of a laboratory shaker that achieves a specified orbital (centripetal) acceleration.

Example 1:

Given parameters for shaker 1

- Desired orbital acceleration: $a = 5 \text{ m/s}^2$
- Orbit radius: $r = 25 \text{ mm} = 0.025 \text{ m}$

Step 1: Use the formula for centripetal acceleration

Centripetal acceleration is defined as:

$$a = \omega^2 \cdot r$$

Solving for angular velocity ω :

$$\omega = \sqrt{a / r} = \sqrt{5 / 0.025} = \sqrt{200} \approx 14.14 \text{ rad/s}$$

Step 2: Convert angular velocity to RPM

The relationship between angular velocity ω and RPM is:

$$\text{RPM} = (\omega \cdot 60) / (2\pi)$$

Substituting the value:

$$\text{RPM} = (14.14 \cdot 60) / (2\pi) \approx 848.4 / 6.2832 \approx 135$$

Conclusion

To achieve an orbital acceleration of 5 m/s^2 with a shaker radius of 25 mm, the required RPM is approximately 135.

Example 2:

Given parameters for shaker 2

- Desired orbital acceleration: $a = 5 \text{ m/s}^2$
- Orbit radius: $r = 15 \text{ mm} = 0.015 \text{ m}$

Step 1: Use the formula for centripetal acceleration

Centripetal acceleration is defined as:

$$a = \omega^2 \cdot r$$

Solving for angular velocity ω :

$$\omega = \sqrt{a / r} = \sqrt{5 / 0.015} = \sqrt{333} \approx 18.26 \text{ rad/s}$$

Step 2: Convert angular velocity to RPM

The relationship between angular velocity ω and RPM is:

$$\text{RPM} = (\omega \cdot 60) / (2\pi)$$

Substituting the value:

$$\text{RPM} = (18.26 \cdot 60) / (2\pi) \approx 1095 / 6.2832 \approx 175$$

Conclusion

To achieve an orbital acceleration of 5 m/s^2 with a shaker radius of 15 mm, the required RPM is approximately 175.

Therefore, the angular velocity (RPM) of each shaker in a study should be adjusted depending on the orbital radius of the respective shaker to result in comparable dislodging efficiency. The following table provides a summary of orbital radii of given shakers and the corresponding angular velocity in RPM that provides comparable dislodging efficiency. The mathematical equations to derive the following table are presented in this appendix.

Orbital radius [mm]	5	10	15	20	25	30	40	50	60
RPM (approx.)	300	215	175	150	135	125	110	95	85

Appendix C - *Field samples must not be corrected for both field and lab recoveries*

The double correction problem

Correcting field samples for both field recoveries and lab recoveries creates a systematic overcorrection that inflates analyte concentrations beyond their true environmental levels. This practice fundamentally misunderstands the relationship between these two recovery measurements and leads to inaccurate data interpretation.

Field recoveries already incorporate lab losses

Field recovery samples (fortified samples collected and processed identically to field samples) experience the complete analytical journey:

- Collection and handling procedures (e.g., environmental conditions, same water/solvent as test samples)
- Transport conditions and duration (e.g., same duration, temperature, agitation)
- Storage conditions and timeframes (e.g., temperature fluctuations)
- Time-dependent degradation
- Matrix-specific interferences that develop during storage
- Laboratory extraction processes (e.g., solvent batches, extraction equipment, lab personnel)
- Instrumental analysis and sensitivity (e.g., instrument type/manufacturer, column type/age)

Any losses observed in field recoveries already include both field-related degradation/loss and laboratory method inefficiencies. The field recovery represents the net recovery of the entire process from sample collection through final analysis. If there were no losses during the field or analytical phase, field recoveries would be 100%.

Lab recoveries measure only method efficiency

Laboratory recoveries (matrix spikes or reference materials) measure solely the analytical method performance under controlled laboratory conditions and are run alongside analytical samples to show method performance was maintained throughout the run. They account for:

- Laboratory extraction processes (e.g., solvent batches, extraction equipment, lab personnel)
- Instrumental analysis and sensitivity (e.g., instrument type/manufacturer, column type/age)

However, procedural recoveries do not account for:

- Collection and handling procedures (e.g., environmental conditions, same water/solvent as test samples)
- Transport conditions and duration (e.g., same duration, temperature, agitation)
- Storage conditions and timeframes (e.g., temperature fluctuations)
- Time-dependent degradation
- Matrix-specific interferences that develop during storage

The correct approach: Field fortification recoveries only

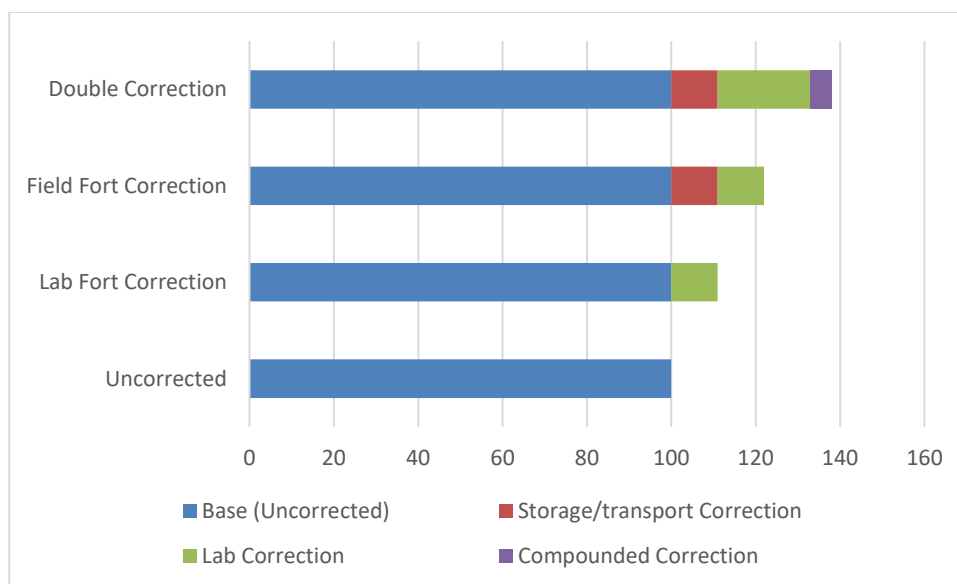
Field fortification samples provide the most accurate correction factor because they:

- Mirror actual sample conditions - Experience identical collection, transport, and storage as field samples
- Include all loss mechanisms - Account for both environmental and analytical losses in a single measurement
- Reflect real-world variability - Capture the true uncertainty associated with the complete analytical process
- Prevent overcorrection - Avoid the mathematical error of correcting for lab losses twice

Mathematical reality

If a field recovery shows 80% recovery and lab recovery shows 90% recovery, correcting by both factors (dividing by $0.80 \times 0.90 = 0.72$) assumes these losses are independent and additive. In reality, the 80% field recovery already includes the 10% lab loss, making the true correction factor simply 0.80, not 0.72.

The mathematical reality is illustrated graphically below, clearly demonstrating the double-counting of lab correction factors. The chart also reveals how sequential corrections compound multiplicatively (similar to compound interest), amplifying the overcorrection beyond what either factor would produce individually.



Conclusion

Using only field fortification recoveries for sample correction provides the most scientifically sound and environmentally representative results. This approach eliminates double counting of analytical losses while properly accounting for all real-world factors affecting sample integrity from collection through analysis.

Appendix D - Examples of DFR derivation

Deriving DFR_X value from a data set

A three-application DFR trial data set is provided below, samples are taken before and after applications. This trial provides 13 different DFR_X values from DFR_0DAA1 to DFR_14DALA and everything in between. Typically, DFR_X values that could be used for submission are the DFR_X values derived after each application. The DFR_X can be defined as the geomean of the sampling replicates.

$$\text{DFR}_{0\text{DAA}1} = 0.36250 \mu\text{g}/\text{cm}^2 \text{ (geomean)}$$

$$\text{DFR}_{0\text{DAA}2} = 0.38314 \mu\text{g}/\text{cm}^2 \text{ (geomean)}$$

$$\text{DFR}_{0\text{DALA}} = 0.43733 \mu\text{g}/\text{cm}^2 \text{ (geomean)}$$

These DFR_X values are GAP specific and can only be used to support GAPs where the rates are equal or lower. For example, DFR_0DAA1 ($0.36250 \mu\text{g}/\text{cm}^2$) could not be used to support a 2-application use of 0.5 kg a.s./ha with an interval of 7 days. Instead DFR_0DAA2 ($0.38314 \mu\text{g}/\text{cm}^2$) should be used.

Trial GAP:

Application rate = 0.5 kg a.s./ha

Number of applications = 3

Interval between applications = 7 days

Entry	Actual Sample Interval (days)	Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Residue ($\mu\text{g}/\text{cm}^2$)
1	0 DBA1	0.00012	0.00005
2		0.00004	
3		0.00003	
4	0 DAA1	0.38298	0.36250
5		0.37433	
6		0.33228	
7	0 DBA2	0.02549	0.02814
8		0.03190	
9		0.02739	
10	0 DAA2	0.41637	0.38314
11		0.38972	
12		0.34660	
13	0 DBA3	0.04172	0.05022
14		0.05644	
15		0.05378	
16	0 DALA	0.46364	0.43733
17		0.40296	
18		0.44770	
19	8 HALA	0.34085	0.37431

Entry	Actual Sample Interval (days)	Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Residue ($\mu\text{g}/\text{cm}^2$)
20		0.39670	
21		0.38786	
22		0.28320	
23	1 DALA	0.27447	0.27371
24		0.26380	
25		0.16713	
26	2 DALA	0.15773	0.16123
27		0.15897	
28		0.12304	
29	3 DALA	0.13779	0.12063
30		0.10354	
31		0.11322	
32	5 DALA	0.07284	0.09082
33		0.09083	
34		0.05643	
35	7 DALA	0.07228	0.05232
36		0.03511	
37		0.02459	
38	10 DALA	0.03184	0.02790
39		0.02774	
40		0.01403	
41	14 DALA	0.01497	0.01463
42		0.01490	

Deriving DFR_{NORM} from a 1 app data set

DFR_{NORM} values can be derived by taking into account the application rate. These DFR values can be considered independent to the GAP and should be taken immediately after application.

In this trial the DFR_{NORM} is the DFR_X [$\text{DFR}_{0\text{DAA}1}$ ($\mu\text{g}/\text{cm}^2$)] / Application rate (kg a.s./ha) = $0.36250 \mu\text{g}/\text{cm}^2$ / 0.5 kg a.s./ha = $0.72501 \mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$

$$\text{DFR}_{\text{NORM}} = 0.72501 \mu\text{g}/\text{cm}^2/\text{kg ai/ha (geomean)}$$

Trial GAP:

Application rate = 0.5 kg a.s./ha

Number of applications = 1

Interval between applications = NA

Entry	Actual Sample Interval (days)	Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Residue ($\mu\text{g}/\text{cm}^2$)	Application rate (kg a.s./ha)	DFR_{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)	Geomean DFR_{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)
1	0 DBA1	0.00012	0.00005	NA	NA	NA
2		0.00004			NA	

Entry	Actual Sample Interval (days)	Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Residue ($\mu\text{g}/\text{cm}^2$)	Application rate (kg a.s./ha)	DFR _{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)	Geomean DFR _{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)
3		0.00003			NA	
4	0 DAA1	0.38298	0.36250	0.5	0.76596	0.72501
5		0.37433			0.74866	
6		0.33228			0.66457	

Deriving DFR_{NORM} from a three-application data set, replicate combinations

Multiple DFR_{NORM} values can be derived from DFR studies with multiple applications.

The DFR_{NORM} from Application 1 can be calculated as above, the DFR_{NORM} from Application 2 and Application 3 require some more data processing to remove the impact of the previous applications on the DFR (essentially resetting the foliar residues to zero before second, third applications). In the below table this is done by taking away the geomean DFR_ODBA2 from DFR_ODAA2 and taking away the DFR_ODBA3 from the DFR_ODAA3 (under the column single app residue). These values can then be normalised for application rate by dividing these values by the application rate.

App 1 - DFR_{NORM} = 0.72501 (geomean)

App 2 - DFR_{NORM} = 0.71000 (geomean)

App 3 - DFR_{NORM} = 0.77423 (geomean)

Overall Geomean DFR_{NORM} = 0.735906 (geomean)

Trial GAP:

Application rate = 0.5 kg a.s./ha

Number of applications = 3

Interval between applications = 7 days

Entry	Actual Sample Interval (days)	Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Residue ($\mu\text{g}/\text{cm}^2$)	Single app Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Single app Residue ($\mu\text{g}/\text{cm}^2$)	Application rate (kg a.s./ha)	DFR _{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)	Geomean DFR _{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)
1	0 DBA1	0.00012	0.00005	NA	NA	0.5	NA	NA
2		0.00004		NA			NA	
3		0.00003		NA			NA	
4	0 DAA1	0.38298	0.36250	0.38298	0.36250	0.5	0.76596	0.72501
5		0.37433		0.37433			0.74866	
6		0.33228		0.33228			0.66457	
7	0 DBA2	0.02549	0.02814	NA	NA	0.5	NA	NA
8		0.03190		NA			NA	

Entry	Actual Sample Interval (days)	Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Residue ($\mu\text{g}/\text{cm}^2$)	Single app Residue ($\mu\text{g}/\text{cm}^2$)	Geomean Single app Residue ($\mu\text{g}/\text{cm}^2$)	Application rate (kg a.s./ha)	DFR _{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)	Geomean DFR _{NORM} ($\mu\text{g}/\text{cm}^2/\text{kg a.s./ha}$)
9		0.02739		NA			NA	
10	0 DAA2	0.41637	0.38314	0.38823	0.35500	0.5	0.77647	0.71000
11		0.38972		0.36158			0.72317	
12		0.34660		0.31846			0.63692	
13	0 DBA3	0.04172	0.05022	NA	NA	0.5	NA	NA
14		0.05644		NA			NA	
15		0.05378		NA			NA	
16	0 DALA	0.46364	0.43733	0.41342	0.38711	0.5	0.82685	0.77423
17		0.40296		0.35274			0.70549	
18		0.44770		0.39748			0.79496	

Deriving DFR_{NORM} from a two-application data set without pre-application samples

In some cases, trials may have received multiple applications before a sample is taken and it is therefore unknown how much residue was remaining from previous applications. In this case the DT₅₀ can be used to derive a multiple application factor (MAF).

The MAF takes into account the degradation of previous application residues and can be used to estimate the total application rate that a plant has received by multiplying the application rate by the MAF.

A DFR_{NORM} can now be accurately derived by dividing the DFR_X by the MAF adjusted application rate because we can relate the DFR from multiple application to a predicted application rate.

If we were to simply divide the DFR_X by the last application rate this would overestimate exposure because it would not consider DFR left over from previous applications.

If we were to divide the DFR_X by the total application rate we would underestimate DFR_{NORM} because this would not take into account, the degraded residue from the leaf surface.

An example of how to use the MAF to derive the DFR_{NORM} is shown below:

MAF derivation:

$$\text{MAF adjusted 2 app rate} = [\text{Dose A1} \cdot e^{-k \cdot t_1}] + [\text{Dose A2} \cdot e^{-k \cdot t_2}]$$

Where $k = \ln(2)/\text{DT}_{50}$, t_1 = time interval between A1 and A2, and $t_2 = \text{zero}$

The GAP followed was 2 x 0.5 kg a.s./ha with 7-day interval and a DT₅₀ of 7 days.

$$\text{MAF adjusted 2 app rate} = [0.5 \text{ kg a.s./ha} \cdot e^{-\ln(2)/7 \cdot 7}] + [0.5 \text{ kg a.s./ha} \cdot e^{-\ln(2)/7 \cdot 0}] = 0.25 \text{ kg a.s./ha} + 0.5 \text{ kg a.s./ha} = 0.75 \text{ kg a.s./ha}.$$

So, for this example the MAF adjusted rate = 0.75 kg a.s./ha

DFR_{NORM} derivation

$$\text{DFR}_{\text{NORM}} = \text{DFR}_{\text{ODAA2}} / \text{MAF}_{\text{AR}}$$

$$\text{DFR}_{\text{NORM}} (\text{Geomean}) = 0.38314 \mu\text{g}/\text{cm}^2 / 0.75 \text{ kg a.s.}/\text{ha} = \mathbf{0.51085 \mu\text{g}/\text{cm}^2/\text{kg a.s.}/\text{ha}}$$

Trial GAP:

Application rate = 0.5 kg a.s./ha

Number of applications = 2 (application interval = 7 days)

Measured DT₅₀ = 7 days

Entry	Actual Sample Interval (days)	Residue (µg/cm ²)	Geomean Residue (µg/cm ²)
1	0 DAA2	0.41637	0.38314
2		0.38972	
3		0.34660	

Appendix E - Abbreviations and Acronyms

- **a.s.** - active substance
- **BBCH** - Biologische Bundesanstalt, Bundessortenamt und CHemische Industrie (Growth stage scale)
- **BW** - Body Weight
- **C** - Control (plot)
- **CAKE** - Computer Assisted Kinetic Evaluation
- **CGMS** - Crop Growth Monitoring System
- **CLE OBE TSG** - CropLife Europe Occupational and Bystander Exposure Technical Subgroup
- **DA** - Dermal Absorption
- **DAA** - Day(s) After Application
- **DALA** - Day(s) After Last Application
- **DBA** - Day(s) Before Application
- **DFR** - Dislodgeable Foliar Residues
- **DFR₀** - DFR at time zero
- **DFR_{DEF}** - Default DFR
- **DFR_{NORM}** - Normalised DFR
- **DFR_X** - DFR at specific time point X
- **DFOP** - Double First Order in Parallel
- **DT₅₀** - Dissipation Time 50 (half-life)
- **DT₉₀** - Dissipation Time 90
- **EFSA** - European Food Safety Authority
- **EPA** - Environmental Protection Agency
- **EU** - European Union
- **FOCUS** - Forum for the Co-ordination of pesticide fate models and their use
- **FOMC** - First Order Multiple Compartment
- **GAP / GAPs** - Good Agricultural Practices
- **GD** - Guidance Document
- **GLP** - Good Laboratory Practice

- **HAA** - Hour(s) After Application
- **HALA** - Hour(s) After Last Application
- **HS** - Hockey Stick
- **JRC** - Joint Research Center
- **KinGUI** - Kinetic Graphical User Interface
- **LOD** - Limit of Detection
- **LOQ** - Limit of Quantification
- **MAF** - Multiple Application Factor
- **MARS** - Monitoring Agricultural Resources (JRC database)
- **n.d.** - not detected
- **NEU** - Northern Europe (zone)
- **OECD** - Organisation for Economic Co-operation and Development
- **OPPTS** - Office of Prevention, Pesticides and Toxic Substances
- **PMRA** - Pest Management Regulatory Agency
- **PPPs** - Plant Protection Products
- **SEU** - Southern Europe (zone)
- **SFO** - Single First Order
- **T** - Treated (plot)
- **TC** - Transfer Coefficient