

Efficacy Guideline 303

Effects on Non-Target Crops of Highly Active Herbicides - Including Mixtures and Sequences

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Contents

Introduction.....	2
Aim of the guideline	2
Preliminary testing of biological activity	2
Succeeding crops.....	3
Problem	3
Extent of testing needed	3
Joint application to the same crop of two ALS.....	4
Data required.....	4
Circumstances when more limited testing may be acceptable.	5
Methods of analysis.....	5
Adjacent crops – spray drift	5
Adjacent crops - spray tank cleaning.....	6
Problem	6
Need for testing.....	6
Adjacent crops – vapour drift.....	6
Crop safety and effectiveness testing	7
General	7
Resistance.....	7
Label agreement and data access	7
Checklist.....	7
Further information.....	8

Introduction

From the 1980s onwards sulfonylurea and other highly biologically active herbicides were introduced that could be applied at only a few grams per hectare. The mode of action of these herbicides is mostly by inhibition of acetolactate synthase (ALS).

These herbicides have two main characteristics:

- They have a great difference in tolerance, up to 20,000 fold, between the most and least sensitive plant species.
- They are active by foliar and root uptake with some degree of soil persistence.
- Because of these attributes they make very useful herbicides for removing sensitive species from tolerant crops. However, because of their activity they can cause adverse effects in non-target crops, such as:
 - Succeeding crops grown on the treated field - due to residues persisting in the soil.
 - Adjacent crops grown in neighbouring fields – due to spray drift
 - Subsequently treated crops – due to residues remaining in the application equipment due to ineffective cleaning.

Although the first few ALS herbicides were applied to cereal crops for control of broad-leaved weeds these herbicides are very variable in their activity against plant species. Crops that can now be treated include sugar beet, linseed, maize, grassland, oilseed rape and potatoes. Different ALS herbicides have activity against grass and broad-leaved weeds, both annual and perennial.

Aim of the guideline

The aim of this guideline is to provide guidance on the types of efficacy testing needed to investigate effects on non-target crops in order to support an application for approval of an active substance of this nature. These requirements were first introduced under COPR but have been reinforced by newer efficacy requirements. These requirements would apply to any herbicide that is highly biologically active but as most herbicides of this nature are ALS inhibitors the term 'ALS' will be used in the guideline

Application of two ALS herbicides applied as either a sequence or tank-mixture can pose a greater risk to adjacent and succeeding crops than applying a single such compound. This guideline outlines these concerns and the data required to address them. Use on the same crop in mixture or sequence will be referred as 'joint application' for the purpose of this guideline.

Advice is also given as to where to find information on other areas that must be considered when recommending mixtures and sequences, see section 0.

Preliminary testing of biological activity

To understand the potential for adverse effects it is very important that a good understanding of the level of biological activity is sought for each ALS. Pre-and post-emergence selectivity across a range of representative crop species should be ascertained from glasshouse or semi-field testing. NOEL or ED₁₀ values are needed for the most sensitive species in comparison to those for a tolerant crop. This information is invaluable as, using exposure estimates from other work such as fate and behaviour or spray drift studies, the need for further laboratory and field-testing in several areas can be determined. If a range of crops is screened then representative worst case crops can be included in the various field studies conducted and extrapolation to other less sensitive crops can be made. In the absence of the preliminary biological activity testing then a full range of crop species will need to be included in the various types of field trials required.

There are no specific EPPO guidelines on these studies. EPPO standard PP 1/207 'Effects on succeeding crops' gives information on screening for pre-emergence activity and refers to suitable test methods. For post-emergence screening suitable protocols should be followed where available or drawn up where necessary. OECD Guideline 208 'Terrestrial (Non-target) Plant Test: Part B Vegetative Vigour Test' suggests methods for screening of activity against emerged plants.

Succeeding crops

Please note: This guidance must be read in conjunction with EPPO Guideline PP 1/207 'Effects on succeeding crops', which provides full details of succeeding crops trial requirements.

Problem

In general ALS pose a risk to succeeding crops due to their very high biological activity in soil, rather than because of any particularly greater persistence in soil than other types of active substance. Another characteristic of some of these ALS active substances is that, because they are weak acids, some can dissociate at higher pH becoming more mobile and sometimes more persistent. This means that soil characteristics, particularly soil pH, can have a great effect on the risk ALS pose to following crops.

EPPO Guideline PP 1/207 describes the testing required for any individual active substance. Factors taken into account when deciding on the extent of testing required include the crops identified in biological screening as being particularly sensitive, and the soils identified as providing a high risk of carry over of biologically active levels of the active substance or metabolites. EPPO PP 1/207 recommends that a suitable standard is included in the trials to indicate whether the conditions during the trial were conducive to carry-over of a similar type of herbicide. It can also be useful to apply a standard treatment known to cause carry-over problems, or to apply a product at much higher than recommended dose, e.g. 4N or 6N, as a 'negative' standard to indicate that a particular trial was conducted in conditions where some carry-over might have occurred. If no damage is seen with the negative standard then it is considered that conditions were not conducive to carry-over, and the results of such a trial would be of limited value.

Extent of testing needed

The extent of testing required depends on the degree of risk to succeeding crops identified. Where a high risk is identified, testing over at least two years would be

required, so that a range of conditions should be encountered including those shown to be high risk. At least four specific following crop trials should be carried out each year looking at effects on a range of test crops planted at each site, with application at single and double (2N) doses. This information should be supported by evidence from effectiveness and particularly crop safety trials (because 2N would have been applied) where the succeeding crop is examined for any effects. EPPO 207 also describes other types of trial that can usefully be carried out. Further detailed trials examining effects on yield may be required where visual effects are seen on particular crops in these field trials, and the applicant does not wish to specify restrictions on the planting of these crops on the label.

Joint application to the same crop of two ALS

With joint application there is a risk of additive effects where a succeeding crop is planted which is particularly sensitive to both ALS. The risk is that both herbicides could persist under the same soil conditions in biologically active quantities until such time as the succeeding crop is planted. Studies submitted to CRD have confirmed that in some circumstances joint application can cause greater damage to certain succeeding crops than when the same active substances are applied alone to separate plots. Regulatory action in this area was not due, as is sometimes stated, to any consideration that the presence of one ALS interferes with the degradation of another ALS or that there is synergistic action between the two ALS. Action has been on based on consideration of additive activity.

As a result of these potential problems the Advisory Committee on Pesticides at its January 1994 meeting agreed that the labels of all sulfonylurea herbicides must contain the instruction that they should not be used in mixture or sequence with any other product containing a sulfonylurea. The ACP also agreed that all sulfonylurea herbicides should be identified as such on the product labels, so that users could comply with this advice. Since that time other ALS inhibitors have been approved which are not sulfonylureas but have similar activity. Where an ALS is identified as having similar activity to the sulfonylureas, then a warning has been added to the label preventing use in mixture and sequence with other ALS herbicides, including sulfonylureas.

Data required

To remove the label restriction against joint application with any other ALS then data would normally be required. These data need to support any specific statement made on the label about which crops can be grown after stated intervals following joint ALS application. Alternatively, if all crops can be sown following joint application then evidence must be provided that a range of crops, particularly those most sensitive to either ALS, can be grown after the usually expected interval between application and planting a succeeding crop.

Work carried out over two cropping seasons should be submitted. Field trials should include the crops that are most sensitive to each active substance together with any that are reasonably sensitive to both. Trials should be carried out where soil conditions are such that greater persistence of the two herbicides would be expected. It would be expected that at least three specific trials examining a range of crops should be conducted each year to demonstrate that the joint application poses no greater risk than when the individual active substances are applied alone, or to support any specific label advice given.

Circumstances when more limited testing may be acceptable.

There can be certain circumstances where more limited testing might be needed for joint application of ALS herbicides, these include:-

- Where certain crops are very tolerant to both ALS being jointly applied, e.g. where both ALS can be applied to the same cereal crops. These crops could be accepted as suitable following crops with very limited work. However, work would still be needed to demonstrate the interval required before more sensitive crops could be grown.
- Where the biological activity of the two compounds is very different, such as joint application of two ALS, one that only has activity against broad-leaved plants the other only being active against grasses.
- Where the persistence of the two ALS is enhanced by different soil conditions, one persisting longer at high pH the other at low pH.

If only limited testing is conducted then a fully argued case must be supplied with any application for approval.

Methods of analysis

With previous considerations of the potential for sulfonylurea herbicides to damage following crops, the provision of a sufficiently sensitive method of analysis for the detection of residues in soil was seen as a key requirement. The limit of detection needs to be at or preferably below the lowest level that causes crop damage; otherwise it would be difficult to investigate whether the effect was due to the presence of a certain active substance or some other factor. With joint application the method should be specific so as to detect the presence of the one ALS applied in the presence of the other.

Adjacent crops – spray drift

With sufficient screening of post-emergence biological activity it is unlikely that any specific field tests will be required to address this area. Predictions of the extent of spray drift can be taken from standard models; these can be compared to the level of biological activity in order to predict the likelihood of an effect at different distances from the treated crop. Because of their high level of activity it is likely that with ALS there will be a risk to adjacent crops unless they are applied very carefully to minimise or prevent drift. As a result, to address this area a strong label warning is normally required, such as:

‘Extreme care is required to avoid drift onto non-target crops’.

Depending on the predicted risk from an individual active substance the wording can be adjusted accordingly.

When considering mixtures of two ALS it is likely such a warning will already be present on at least one of the product labels, this warning will then also apply to the mixture. If no such warning is present on the label of either product it may be necessary to carry out an assessment on the mixture to see if joint application leads to a greater risk and

therefore such a warning is necessary for the mixture.

Adjacent crops - spray tank cleaning

Problem

As ALS are active at such low levels a spray tank cleaning method must be extremely thorough so that damaging levels of an active substance do not remain in the tank after cleaning. Tank mixtures, where the loading of ALS in the spray tank is higher, pose an even greater risk.

Because of their activity, specific spray tank-cleaning methods have been developed for ALS products. Methods based on sodium hypochlorite were first used to help tank washing. Even using this method, with some ALS, problems were still seen when tank mixed with other products, particularly emulsifiable concentrates. In these cases deposits that were not soluble in water were formed and these adhered to the surfaces of spray tanks. Later when spraying other crops such as sugar beet, products containing strong organic solvents were added to the spray tank. These solvents removed the ALS deposits from the walls of the spray tank leading to severe damage in the sensitive crop being treated. Tank washing using an ammonia-based product was successfully introduced to help overcome the problem of insoluble deposits.

Need for testing

All single active products and mixtures of ALS (both formulated and tank-mixtures) which are recommended or stated to be compatible on the label should be tested. Three-way mixtures with other products should also be examined if they appear on the label. With ALS, worse case mixtures have usually involved emulsifiable concentrates. Any worse case mixtures for the individual ALS should be tested. If the test method proves not to be suitable for some mixtures then use of these can be prohibited on the label or use can be restricted to a positive list of acceptable three-way mixtures.

As stated, different ALS can have different tank cleaning methods. Both methods can be tested and if necessary the most suitable method should be recommended on the label for that product or mixture. A combination of methods using sodium hypochlorite and ammonium must be avoided as this could lead to the production of noxious gases.

Adjacent crops – vapour drift

Data on physical chemical properties and observations made in screens and field trials should indicate whether there is a potential for vapour drift. Where this indicates risk is low a case should be provided. Where a risk is indicated then specific trials should be set up to examine the extent of damage that can be seen on neighbouring sensitive crops. In these trials application can be made to an area of crop at times when conditions after application are likely to be conducive to vapour drift. Careful observation should be made for effects on neighbouring crops and other vegetation, including weeds. Sensitive species grown in pots can be placed in and at set distances around the sprayed area shortly after application. These plants should be closely monitored for any damage. If a risk is identified then advice should be included on the label so that the product is only applied at a sufficient distance from sensitive crops to prevent damage occurring. Any advice drawn up should be of a reasonable nature so that it is possible for a user to comply with the instructions given, taking into account

Efficacy Guideline 303 Version 1.1 July 2020

that fields surrounding a treated field may be owned by a different grower. Where an active substance is soil acting the advice given should encompass situations where vapour might drift onto bare land yet to be planted with a crop.

Unless both active substances have the potential to cause damage by vapour drift further data would not be required to support joint application. If both can cause damage in this way then the possibility of additive effect must be addressed. In general with ALS herbicides no problems with vapour drift have been seen.

Crop safety and effectiveness testing

General

For any single active product or formulated mixture the usual evidence of effectiveness and crop safety data will be required in line with the EPPO standards.

For tank-mixtures and sequences with other products see CRD [Efficacy Guideline 604](#) 'Efficacy data required for tank mixtures and sequences of pesticides'.

Resistance

Application to the same crop of two ALS herbicides that are active against the same weeds can increase the selection pressure and therefore the risk of resistance development, especially when applied in sequence. Where joint application is to be made possible, for convenience, or positively recommended on the label, then any resistance risk assessment made and any resistance management plan previously implemented must be reconsidered in light of the joint application. For further information see EPPO Guideline PP 1/213.

Label agreement and data access

When a mixture or sequence is first considered, for the reasons given at 2 above, this will be prohibited on both product labels. If this restriction is only removed from one label this will be confusing for users. Use is still acceptable, being in line with one of the labels, but liability for this use may be unclear. To make it clear to a user that joint application is acceptable, when the first product's label is amended a parallel application should be made to amend the label of the second product.

To support a mixture or sequence it is usually necessary or preferable to have access to the data that supports the approval of both products. Then the data on biological activity and persistence of both active substances can be referenced during evaluation. Otherwise the application must stand-alone for one of the herbicides, with no background information being available from previous applications. As a result detailed testing over a range of crops and timings is likely to be needed. This is because for one of the herbicides cases cannot be supplied for a lesser extent of testing on the grounds of biological activity or soil conditions. Alternatively, data on one of the active substances can be supplied from other sources, such as the public domain.

Checklist

- Carry out screening in order to understand the relative biological activity and persistence of the one or more ALS to be applied.

Efficacy Guideline 303 Version 1.1 July 2020

- If necessary, carry out field trials looking at effects on succeeding crops, take into account crop susceptibilities and persistence of the ALS(s) to be applied when designing trials.
- Conduct laboratory tests examining whether recommended tank-cleaning methods remove biologically active traces of single or mixtures of ALS herbicides, including when mixed with a third product, particularly an emulsifiable concentrate.
- Consider the need for field trials examining crop safety and weed control of any ALS mixture/sequence, the extent depending on whether it is a convenience or a positively recommended mixture/sequence.
- For mixtures and sequences, if possible, make applications for the amendment of both product labels, so that the situation is clear to users when reading either label.

Further information

For information about health and safety, or to report inconsistencies or inaccuracies in this guidance, visit www.hse.gov.uk.

This guidance is issued by the Health and Safety Executive. Following the guidance is not compulsory, unless specifically stated, and you are free to take other action. But if you do follow the guidance you will normally be doing enough to comply with the law. Health and safety inspectors seek to secure compliance with the law and may refer to this guidance.

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