Efficacy Guideline 617

Re-registration of Triazole uses in cereals: fungicide resistance issues

Contents

Background

Triazole and other DMI fungicides have been available for many years and as a result resistance has developed in a wide range of pathogens. These include some major cereal diseases including *Septoria tritici*, powdery mildew, *Rhynchosporium* and possibly Net blotch. This resistance may have caused the performance of products to decline and as a result we cannot simply re-register claims for these diseases based on old COPR data.

This document provides advice to applicants on how CRD will consider the 'triazole decline' issue at re-registration including advice on the data relevant to this issue required at re-registration.

DMI fungicides

The demethylation inhibitors (DMIs) include not only the triazoles but also the imidazole and pyrimidine fungicides (also the piperazine and pyridine fungicides triforine and pyrifenox but these are not registered in the UK). While there are some differences in performance it is generally accepted that there will be cross-resistance between the different DMI chemical groups. However, resistance to one DMI does not always lead to resistance in another.

DMIs are part of the wider Sterol biosynthesis inhibitors (SBI) but there does not appear to be any cross resistance between the different SBI groups.

UK registered DMI fungicides:

Imidazole Chemical Group:
- Imazalil
- Prochloraz

Pyrimidine Chemical Group:
- Fenarimol

Triazole Chemical Group:
- Bitertanol
- Bromuconazole
- Cyproconazole
- Difenoconazole
- Epoxiconazole
- Fenbuconazole
- Fluquinconazole
- Flusilazole
- Flutriafol
- Ipconazole
- Metconazole
- Myclobutanil
- Penconazole
- Propiconazole
- Prothioconazole
- Tebuconazole

- Tetraconazole
- Triadimenol
- Triticonazole

Resistance in DMIs

Resistance to DMIs is multistep, caused by a range of different mutations (polygenic) that result in a progressive loss of sensitivity. Complete loss of performance is therefore unlikely.

Recent research on *Septoria tritici*, including that conducted under a LINK project (LK0976 Triazole resistance in UK populations of *Mycosphaerella graminicola*) has identified a number of specific mutations that appear to be linked to resistance. This work also shows that there are differences between the triazoles with some being more affected than others, a fact backed up by some field trials funded by PSD that looked at the comparative performance of triazoles against *Septoria tritici* (PS2711 Assessing the performance of azole fungicides against *Septoria tritici*). The graph below shows the mean eradicant and preventative activity on the flag leaf, across four sites, for all triazoles sold at the time for use on cereals in the UK. Other assessments give slightly different rankings for individual fungicides. A summary is available on the CRD website at Triazole Septoria Trials - Final Report.

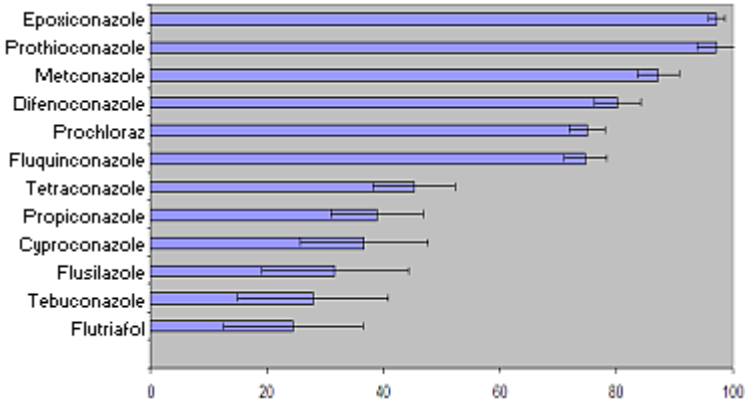

Figure 1; Control of S. tritici by different DMIs

The data are limited in that they are only from four sites over a single year and only one product was tested for each active substance. In the absence of any other evidence CRD will rely on them to determine what an appropriate control claim for a given product may be. They do indicate that the performance of some products may be severely affected, and existing claims may not be appropriate and will need to be reconsidered at re-registration

Regulatory action

The labelling of DMI fungicides used in cereals to must include the following advice (announced in Regulatory update 17/2007):

> *[Name of Product] contains a DMI fungicide. Resistance to some DMI fungicides has been identified in Septoria leaf blotch (Mycosphaerella*

graminicola) which may seriously affect the performance of some products. For further advice on resistance management in DMI's, contact your agronomist or specialist advisor, and visit the Fungicide Resistance Action Group (FRAG)-UK website.

Data are also required to support all claims for the control of *Septoria tritici* and any other disease in which resistance has been reported, which included powdery mildew on both wheat and barley and Rhynchosporium. Data should be from recent trials (e.g. 2007 and later) conducted in the UK, and with the test product. Recent public domain evidence from use of the active substance contained in the test product against relevant diseases in the UK would be considered supporting evidence as part of the data set.

Cereal diseases exhibiting resistance to DMIs

Resistance has been confirmed by FRAG in the following cereal diseases.

- Wheat
  - *Septoria tritici* (*Mycosphaerella graminicola*)
  - Powdery mildew (*Erysiphe graminis f.sp tritici*)
  - Eyespot (*Pseudocercosporella herpotrichoides* R-type)
  - Tan spot (*Pyrenophora tritici-repentis*)
- Barley
  - Rhynchosporium (*Rhynchosporium secalis*)
  - Powdery mildew (*Erysiphe graminis f.sp hordei*)
  - Net blotch (*Pyrenophora teres*)

Resistance in Net blotch and Tan spot has not been associated with control failures in the UK. However, recent data submitted to CRD have suggested that this is an issue. Tan spot is a new and minor disease and it is unlikely that there have been significant shifts in performance since any claims were authorised. Eyespot is not a major target for most DMIs.

Although resistance has not been confirmed there have been reports of shifts in the sensitivity of other diseases. The possibility of resistance cannot therefore be excluded for any disease.

Note that there are also many cases of confirmed resistance in pathogens of other, non-cereal, crops.

Additional information on resistance

The position with regards to resistance is not static. Between 2006 and 2009 there appears to have been little further reduction in performance. However, this does not

mean that further reductions will not occur in the future and it is important to ensure that the latest research findings are taken into account.

CRD Action at re-registration

1. Where CRD suspect that the performance of a product may have declined since it was first registered, we will consider whether the existing claims need to be amended or deleted. This includes all the above mentioned diseases.

2. Where a claim was last evaluated more than about five years ago, we will re-consider claims for any disease in the above list of diseases exhibiting resistance.

3. Where more recent data have been considered then we may judge that this is sufficient. Decisions should be made on a case by case basis and take account of recent research findings, particularly historical trends as to when shifts in sensitivity have occurred.

4. If there is evidence to indicate shifts in performance for other diseases we may reconsider those. This may also include non-cereal diseases.

5. If wider scientific opinion is such that action in advance of re-registration is required, then CRD will reconsider the approach outlined in this paper.

6. Where new studies are presented to support the continued use of a product against diseases exhibiting resistance to DMI's these data may be subject to a period of data protection.

Data requirements

Applicants should submit data generated since 2006, on the performance of their product against any of the affected target diseases for which they wish to continue to make a label claim. A full package of ten trials is not necessary. Provided the results are consistent, then as a guide three trials may be adequate if they are broadly in line with the results of the comparative performance field trials or other public domain evidence. However, it is the applicant's responsibility to refer to these in the BAD.

For diseases not currently considered to be affected by resistance, such as *Septoria nodorum* and rusts, CRD can accept that COPR data are still valid unless there is specific evidence to suggest otherwise. Note that this includes diseases such as powdery mildew on rye and oats which are different strains of *Erysiphe graminis* and are not known to exhibit resistance. Triticale is infected by the same strain of powdery mildew as wheat and so claims will be affected but can be extrapolated from wheat if already on the label (and the same as wheat). Where efficacy data are submitted and show consistently lower performance than would be expected the possibility of this being a result of resistance should be considered.

Permissible claims

CRD will not re-register products unless they are sufficiently effective. If as a result of the re-evaluation of claims a product no longer has any claims for 'control' then

consideration must be given to refusing approval completely, at least for use on cereals. In most cases however, DMI fungicides will probably include claims for the control of other diseases, such as rusts, that do not exhibit resistance. In this case claims for moderate control, or reduction, of the diseases exhibiting resistance to DMI's may be permissible provided they are adequately supported. The applicant must consider the data and make appropriate label recommendations in line with the results demonstrated.

CRD will not assume that claims for control will automatically be down graded at re-registration. There is considerable variation in the effectiveness of different DMIs. While there is evidence that the performance of all compounds has reduced to some diseases, some, particularly but by no means exclusively, prothioconazole and epoxiconazole based products may still exert sufficient control to warrant a full control claim.

Mixtures of DMI fungicides

The principals above also apply to all mixture products for foliar use, either combinations of DMIs or mixtures of DMIs plus active substances from other groups, *i.e.* for the diseases affected by resistance, the applicant will need to demonstrate the product is performing in line with the claims made on the label.

Where active substances are mixed to give improved control, data will be required to demonstrate that each component of the mixture is making an effective contribution to control. Overall, the product must meet the minimum effective dose requirements of the Uniform Principles. Where DMIs are used in mixture the impact on resistance management of any increase in total DMI use compared to solo products must be considered.

Where mixtures are for resistance management purposes then consideration will need to be given to whether the DMI component would still provide adequate control if applied alone.

Any other claims, for example claims for improving green leaf area for products containing mixtures of DMI and strobilurin fungicides, must be appropriately supported by data.

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.

This leaflet is available at: http://www.hse.gov.uk/pesticides/resources/G/g617.pdf If you wish to reuse this information visit www.hse.gov.uk/copyright.htm for details.

Published by the Health and Safety Executive 01/2021