

## RESISTANCE RISK ANALYSIS FOR PLANT PROTECTION PRODUCTS

Sakine Ugurlu KARAA AÇ

Karabük University, Engineering Faculty,  
Environmental Engineering Department, 78050 Karabük-TURKEY  
(Corresponding author: sugurlu@hotmail.com)

### Abstract

Resistance is the naturally occurring, inheritable adjustment in the ability of individuals in a population to survive a plant protection product treatment that would normally give effective control. Although resistance can be demonstrated in the laboratory, this does not mean that pest control in the field is reduced. The importance of resistance depends on the target pest(s) and crop(s), and on the relevance of the product among the available control measures. For this reason, resistance must be determined by using standard test methods and monitored for key pests. Resistance can be seen for insecticides, fungicides and herbicides. Detection of resistance, monitoring and assessment of resistance risk are interrelated. The aim of resistance risk analysis is to describe how the risk of resistance to plant protection products can be assessed and systems for risk management can be proposed in the context of official registration of plant protection products. Resistance risk analysis is a two-stage process, composed of resistance risk assessment and resistance risk management.

**Key Words:** Resistance, risk assessment, risk management, pests, plant protection products

### Introduction

Resistance is the naturally occurring, inheritable adjustment in the ability of individuals in a population to survive a plant protection product treatment that would normally give effective control. Practical resistance is the term used for loss of field control due to a shift in sensitivity (OEPP/EPPO, 1988). Loss of performance of a plant protection product because of the development of practical resistance in the target organism and the subsequent need for additional product use to achieve control can be costly to the grower, the crop protection company and the environment. Registration authorities and crop protection companies now recognize that the development of resistance can be minimized by means of suitable management strategies, and that it is in both their interests to protect the efficacy of plant protection products. The registration procedure, before the product is released for full commercial use, is seen to be the point at which appropriate risk management strategies should be agreed and implemented. For example, the harmonized registration procedure of the countries of the European Union (EU, 1991) requires that applicants provide information on the possible occurrence and development of resistance. If there is evidence to suggest that difficulties of control could result from the development of resistance, a management strategy should be proposed that would minimize the likelihood of resistance.

The aim of resistance risk analysis is to indicate to the registration authorities and to applicants for registration what their obligations are with regard to assessing and managing the risk of practical resistance in the target organism(s). These elements are included in the process of resistance risk analysis:

- the concepts of resistance;
- how resistance risk might be assessed;
- how resistance might be managed;
- what data must be supplied to support the conclusion of a resistance risk analysis;

- other data needed on resistance in the registration dossier;
- reaching a registration decision with regard to resistance risk.

In contrast to detection and monitoring of resistance in the field after the fact, resistance risk assessment is predicting the possibility of resistance emerging as a result of using pesticide in a given use environment.

### **Resistance risk analysis**

Resistance risk analysis is a two-stage process, composed of resistance risk assessment and resistance risk management (OEPP/EPPO, 2002). In resistance risk assessment, the inherent risk is first assessed using the characteristics of the pest and the product; the unmodified risk is then evaluated from the inherent risk when the product is applied under unrestricted conditions of use. In resistance risk management, the decision is made whether the unmodified risk is acceptable; if it is, the process can stop. If the unmodified risk is not acceptable, possible modifiers are then analyzed to determine whether they can be used to mitigate the risk. If suitable modifiers exist, the conclusion of the resistance risk analysis will be a resistance management strategy.

A resistance risk analysis procedure is needed for the different reasons:

- 1) The manufacturer of plant protection products to assess the potential risk of the development of resistance if the product is used commercially.
- 2) The manufacturer of plant protection products to decide which management options should be applied if the assessed risk of resistance is considered to be unacceptable.
- 3) The registration authorities to evaluate any risk assessment submitted by the applicant concerning the development of resistance.
- 4) Registration authorities to evaluate the proposed use pattern suggested by the applicant.

The overall management of resistance is a continuous process, starting with the initial assessment of resistance risk, which must be made during product development, and continuing with the selection of appropriate measures before the start of sales, and with the implementation of the measures throughout the commercial use of the active substance.

### **Resistance risk assessment**

In order to assess the risk of resistance in the target pest(s), it is necessary to evaluate the different factors contributing to the risk, i.e. those inherent in the compound and its effect on the pest and those that might result from a particular use pattern.

The inherent risk depends on various factors, some of which are associated with the product and others with the pest. The factors associated with the plant protection product that may favour the development of resistance can include:

- persistent activity;
- single-site mode of action;
- monogenic resistance;
- ease of metabolism.

Those associated with the characteristics of the target pest that may favour the development of resistance can include:

- short life cycle/many generations;
- high fecundity/widespread distribution of progeny;
- high inherent genetic variability;
- existence of a mechanism in the pest to metabolize a range of active substances;
- existence of cross resistance;
- high fitness of resistant strains.

Past experience may also provide a guide to resistance risk; higher risk could be indicated in situations where a target pest has already developed resistance to other active substances or where resistance to the active substance has already developed in other target pests.

The risk of resistance inherent in the plant protection product and the pest can be increased by certain conditions of use. Agronomic risk affects selection pressure on the development of resistance and is influenced by the particular characteristics of the crop, the geographic area in which the product is applied and the use pattern. The factors influencing the agronomic risk includes:

- widely grown crop with short rotations;
- mono cropping or continuous cropping;
- application techniques;
- other cultural practices (e.g. fertilizers, cultivation);
- need for high numbers of applications or long exposure to obtain control, because of the features of the crop environment;
- use of transgenic plants with genes expressing pesticidal activity;
- use of cultivars susceptible to the pest(s);
- geographic isolation of populations preventing the reentry of sensitive forms;
- environmental conditions favouring more frequent generations or higher population densities of the pest;
- exclusive reliance on a single active substance;
- lack of diversity of available control measures.

Some important factors may influence a resistance risk assessment. These are type of compound, mode of action/mechanism of resistance, cross-resistance, characterization of strains and test methods for sensitivity.

The consequence of resistance will be a reduction in the level of effectiveness of the product, which may ultimately limit the usefulness of the product or of its chemical group. The importance of this will depend on the target pest(s) and crop(s), and on the relevance of the product among the available control measures. In addition, the potential consequences are strongly influenced by the level of resistance in the target pest(s) (i.e. the frequency of resistant strains) and, in particular, by the speed at which the resistance develops.

### **Resistance risk management**

Resistance risk management refers to the process whereby, first, the decision is taken whether the risk of and then, if necessary, conditions of commercial use that have the specific purpose of minimizing or delaying the appearance of resistance in the field are selected and applied. These specific conditions of use are termed ‘modifiers’. If it is accepted that the risk of resistance developing to a plant protection product is proportional to the exposure of the pest to the product, then any modifier which reduces that exposure will reduce the risk of resistance developing. To have any chance of success resistance management should be the collective responsibility of manufacturers, regulatory authorities, advisers and growers. Information on the resistance management strategy can be given to growers/advisers in a number of ways: recommendations and restrictions on use may be included on product labels; advisory literature or use campaigns may also be used.

Having determined the magnitude of the risk of resistance, it is then necessary to decide whether this risk is ‘acceptable’ or ‘unacceptable’. In other words, to decide whether the use pattern should be modified to avoid or slow the appearance of resistance. An acceptable risk is one where the magnitude of the unmodified risk of resistance is considered to be so low, when using the proposed use pattern. Whether a resistance risk is considered to be unacceptable can have important consequences for all sellers and users of a plant protection product, since this decision

determines whether modifiers need to be applied. If the decision about acceptability of risk is wrong, it will lead either to the imposition of unnecessary modifiers or the development of resistance in the target population(s) sooner than could have been hoped.

The acceptability of the risk does not only depend on the magnitude of the risk (the combination of the probability of resistance occurring and the consequences if it does), but should also take account of the benefits to be obtained from the use of the plant protection product. For example, a higher level of resistance risk may be accepted if:

- there is a limited availability of suitable alternative means of control of the target pest(s)
- the plant protection product has advantages over other available products.

There is also specific strategies that can be used in a resistance management strategy.

The integrated use of combinations of different modifiers is likely to be most beneficial. The characteristics of the particular pest/product combination that affect resistance development and have been identified in the assessment of resistance risk should be taken into account when deciding on the exact strategy. In addition, the strategy should take account of the overall pest management in the crop concerned.

Use of good plant protection practice (OEPP/EPPO, 1993) and the specific recommendations for individual crops (OEPP/EPPO, 2001), the amount of plant protection product used can be reduced to what is really necessary.

Measures related to the application of the product, frequency of application, timing, dose rate, mixtures and alternations and recommendations on the product label are also other risk management strategies.

When the risk of development of practical resistance is assessed to be low, but it is nevertheless believed that, in certain rare circumstances, use of the product may still lead to the appearance of an undesirable level of resistance, it may be considered unnecessary to require the implementation of modifiers. In that case, the product label can carry a warning to the user that resistance could occur under certain circumstances and the label could offer general advice, such as that the product should not be used too frequently or should be used in combination with other products.

### Conclusion

The consequence of resistance indicates a reduction in the level of effectiveness of the product, which may limit the usefulness of the product or of its chemical group. Specific details on different types of plant protection products must be considered to determine the resistance. A resistance risk assessment may be made when a new compound is proposed for use on a new target pest or a new crop or environment. Resistance risk assessment is carried out by a variety of personnel associated with pesticide discovery, development or use. After assessed the resistance risk, it is necessary to decide resistance management strategies to reduce the risk of resistance. All information about the resistance risk and risk management must be considered registration of the plant protection product.

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