



A herbicide resistance risk matrix

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ARTICLE INFO

Keywords:

Resistance risk assessment
Efficacy evaluation
Herbicides
Integrated weed management
EPPO standard
Pesticide authorisation

ABSTRACT

Herbicide resistance is of increasing concern, especially as there is a lack of new modes of action. An assessment of resistance risk has been a key part of the pesticide authorisation process in most European countries since the early 2000's. However, little guidance is provided on how to quantify these risks. The risk matrix described here presents a quantitative approach to the evaluation of the resistance risk posed by the use of herbicides. The inherent, 'unmodified' risk is first assessed by ranking herbicides and major target weed species on a scale from low to high resistance risk, based largely on published information. In practice, agronomic management practices ('modifiers') will reduce the risk and these are factored into the matrix. Modifiers can include management strategies relating to herbicide use as well as non-chemical methods of weed control. By assigning defined impact factors to possible agronomic modifiers, the overall resistance risk of a herbicide under defined use conditions can be quantified. The approach, although simple, appears robust and produces realistic assessments of the resistance risks associated with four contrasting test scenarios. The aim is to achieve a better harmonisation of herbicide resistance risk assessment across Europe. Although the matrix has a European legislative focus, the approach and principles are relevant in other parts of the world where the extensive use of herbicides is a relatively recent development, and where there is currently limited knowledge and expertise on herbicide resistance and the evaluation of resistance risks.

1. Introduction

Weeds are a major constraint to agricultural production, causing significant agronomic and economic damage. In conventional cropping systems weed populations are most commonly managed with herbicides, although non-chemical methods are also an essential component of Integrated Weed Management (IWM) strategies. Repeated applications of herbicides with similar modes of action exert a strong selection pressure on target weed populations with the consequence that numerous cases of herbicide resistance have evolved worldwide (Powles and Yu, 2010). By August 2018, resistance had been confirmed in 255 weed species in 92 different crop types in 70 countries, affecting the efficacy of 163 different herbicides from 23 of the 26 known herbicide sites of action (Heap, 2018).

The increasing number of resistant weed biotypes is a major concern for agriculture, horticulture and amenity situations, especially as no new herbicide mode of action has been marketed for over 30 years (Duke, 2012; Westwood et al., 2018). Similar scenarios also occur for other plant protection product groups such as insecticides and, to a lesser extent, fungicides. To reduce the risk of resistance development,

and thereby to prolong the period of effective use of plant protection products for the benefit of both producer and end-user, resistance risk has been assessed during the authorisation process in most European countries since the early 2000's. The basis for resistance risk assessment is the EPPO Standard, 'PP 1/213 (4) Resistance risk analysis' (EPPO, 2015). EPPO (European and Mediterranean Plant Protection Organisation) is an intergovernmental organisation responsible for cooperation and harmonisation in plant protection and has 52-member countries in the European and Mediterranean region (EPPO, 2018).

The resistance risk assessment of plant protection products during the authorisation process, as specified for herbicides in the EPPO Standard PP 1/213, includes an evaluation of both the *inherent* and the *agronomic* risk of a herbicide. The *inherent* risk is first assessed using the characteristics of both the herbicide active ingredient(s) and the target weed species. For a herbicide, this includes both the intrinsic mode of action of the active ingredient(s), the known cases of resistance and the mechanisms of resistance and cross-resistance. For the target weeds, consideration is given to both the biological characteristics that may predispose a weed species to evolve resistance (such as length of life cycle; seed production, distribution and longevity; genetic plasticity),

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and to what extent resistance has already been found in that species. The evaluation of the *inherent* resistance risk of both herbicide active ingredient(s) and target weed species results in an assessment of the resistance risk under unrestricted (unmodified) use conditions.

However, the cropping system where the herbicide will be applied and the herbicide use pattern will also impact on the selection pressure imposed on the target weed populations. Hence the *agronomic risk* in the field may well differ from the unmodified resistance risk, especially if specific cultural and agronomic management practices ('modifiers') are applied to minimize the resistance risk. If the unmodified risk is high, the impact of these modifiers is evaluated in order to reduce the risks associated with an unrestricted use. Modifiers can include management strategies relating to herbicide use as well as non-chemical methods of weed control.

Any evaluation of the *inherent* and *agronomic* resistance risk is based, not only on published scientific evidence (e.g. The International Survey of Herbicide Resistant Weeds, www.weedscience.org), but also on expert knowledge. Consequently, applicants submitting dossiers for plant protection authorisation purposes, and the evaluators of those dossiers, are attempting to assess future resistance risks based partly on past evidence of resistance, and partly on expert opinion. Applicants and evaluators are likely to have different priorities and, consequently, may reach different conclusions about the resistance risk. In addition, applicants, especially from companies with limited in-house resistance expertise or less familiar with European agronomic conditions, may be uncertain of how much information on resistance risk is required in any dossier.

The risk matrix described in this paper presents a quantitative approach to the evaluation of the resistance risk posed by the use of a herbicide. Herbicide active ingredients and major target weed species are each ranked on a scale from low to high resistance risk, based largely on published information. By assigning defined impact factors to possible agronomic modifiers, the overall resistance risk of a herbicide under defined use conditions can be quantified. The aim is to achieve a better harmonisation of herbicide resistance risk assessment across Europe for the benefit of applicants seeking to register, or re-register herbicides, evaluators and the end-users. Although the matrix has a European legislative focus, the approach and principles are relevant in other parts of the world where the extensive use of herbicides is a relatively recent development, and where there is currently limited knowledge and expertise on herbicide resistance and the evaluation of resistance risks.

2. Materials and methods

2.1. The resistance risk matrix

This risk matrix is based on the assumption that the evolution of herbicide resistance is critically dependent on the interaction of three factors (Moss, 2017a; Vencill et al., 2014).

- A. the *inherent* risk of the **herbicide**
- B. the *inherent* risk of the **target weed**
- C. the **agronomic management practices** (*modifiers*) used in a given field, including the way the herbicide is used as well as alternative non-chemical methods of weed control.

Examples of the individual components contributing to each of these three main risk factors are presented in Fig. 1.

2.1.1. *Inherent risk of the herbicide*

Most types of herbicides are vulnerable to resistance, although some are more vulnerable than others. The risk posed by a specific herbicide can be estimated from the number of cases of resistance that have evolved to herbicides with the same mode of action (MoA), relative to herbicides with different MoA. In this matrix, the herbicide risk is based

on information in the International Survey of Herbicide Resistant Weeds (Heap, 2018). This regularly updated database provides a global overview of cases of herbicide resistant weeds and is supported by government, academic, and industry weed scientists from over 80 countries worldwide. Within the framework of herbicide evaluation by European authorities, it is the major source of information for the assessment of the inherent resistance risk. To classify herbicide active ingredients according to their inherent resistance risk, active ingredients are assigned to their respective herbicide mode of action group (MoA group) as defined by the Herbicide Resistance Action Committee (HRAC). In their classification system, which is used in Europe and most countries worldwide, there are 25 different herbicide mode of action groups (HRAC, 2018). For each HRAC MoA group, the resistance risk is based on the number of resistance cases worldwide (Table 1). HRAC MoA groups are classified as a:

- **high risk** MoA group if the number of species that has evolved resistance to herbicides in that group account for 10% or more of all resistance cases reported.
- **medium risk** MoA group accounts for 5–10% of resistant species.
- **low risk** MoA group accounts for 1–5% of resistant species.
- **very low risk** is assigned to MoA groups with < 1% of resistant species.

The individual active ingredient(s) of any commercial herbicide mixture should be assessed for their resistance risk. It is unwise to assume that any new herbicide MoA group is automatically 'low' risk simply because it has a novel site of action. It is preferable to consider it as 'high risk' until information is available to better quantify the actual risk. However, if it is closely related to an existing HRAC MoA group, that may be a good indicator of the resistance risk.

2.1.2. *Inherent risk of the target weed species*

The inherent risk of a weed species evolving herbicide resistance is influenced by the biological and genetic characteristics of that species. For example, annual weed species have evolved resistance much more often and more quickly than biennial or perennial weed species (Holt et al., 2013). Annual species place greater reliance on sexual reproduction and have a shorter generation time, resulting in more genetic variation and more rapid resistance evolution. Cross-pollination appears to be more effective in enabling resistance-endowing gene recombination and accumulation, especially for metabolism-based herbicide resistance, compared to self-pollination which can limit the speed and spread of resistance evolution (Maxwell and Mortimer, 1994). However, self-pollination is certainly no barrier to the evolution of herbicide resistance; *Avena* spp. (wild-oats) are predominantly self-pollinating yet herbicide resistance has evolved in 21 countries worldwide (Heap, 2018). Seed production potential also impacts on resistance evolution and development. A weed species that produces more seeds would, in theory, have a greater chance of developing herbicide resistance due to a greater number of genetic combinations that have the potential to produce an individual with a herbicide-resistance trait (Jasieniuk et al., 1996).

The relationship between different plant families and their propensity to evolve resistance is correlated to a large degree with their frequency of occurrence as major weeds (Holt et al., 2013). However, some families (e.g. Poaceae and Brassicaceae) are significantly over-represented in the list of resistant species, relative to their frequency as weeds in general. Although there is only a weak bias at the plant family level, at the individual genus level there is good evidence that some weeds are more prone to evolve resistance than others. Several weed species from each of the genera, *Lolium*, *Amaranthus*, *Conyza* and *Echinochloa*, are some of the most problematic herbicide-resistant weeds worldwide.

Perhaps surprisingly, given the amount of research conducted on herbicide resistance, it remains unclear why resistance evolves faster in

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