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journal homepage: [www.elsevier.com/locate/pest](http://www.elsevier.com/locate/pest)

## IRAC: Mode of action classification and insecticide resistance management

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## ARTICLE INFO

## Article history:

Received 26 September 2014

Received in revised form 13 November 2014

2014

Accepted 14 November 2014

Available online

## Keywords:

Insecticide mode of action

Resistance to insecticides

Insecticide resistance management

Pesticide discovery

Insecticide Resistance Action Committee

Integrated Pest Management (IPM)

## ABSTRACT

Insecticide resistance is a long standing and expanding problem for pest arthropod control. Effective insecticide resistance management (IRM) is essential if the utility of current and future insecticides is to be preserved. Established in 1984, the Insecticide Resistance Action Committee (IRAC) is an international association of crop protection companies. IRAC serves as the Specialist Technical Group within CropLife International focused on ensuring the long term efficacy of insect, mite and tick control products through effective resistance management for sustainable agriculture and improved public health. A key function of IRAC is the continued development of the Mode of Action (MoA) classification scheme, which provides up-to-date information on the modes of action of new and established insecticides and acaricides and which serves as the basis for developing appropriate IRM strategies for crop protection and vector control. The IRAC MoA classification scheme covers more than 25 different modes of action and at least 55 different chemical classes. Diversity is the spice of resistance management by chemical means and thus it provides an approach to IRM providing a straightforward means to identify potential rotation/alternation options.

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## 1. Introduction

Insecticide resistance (see [1–3] for definitions) has been a major factor influencing insect control and pest management for more than half a century. The first paper documenting insecticide resistance was published 100 years ago and involved lime sulfur and the San Jose scale [4]. Thereafter, a few sporadic cases of insecticide resistance were reported through the mid-1940s (Fig. 1, [5]). The introduction of the synthetic organic insecticides (i.e. DDT, cyclodienes and organophosphorus insecticides) in the 1940s lead to great improvements in insecticidal efficacy and spectrum, with the

consequent large scale, expanded use of these new tools for pest insect control. Not surprisingly, there was also a rapid rise in the number of cases of resistance due to extensive, repeated use of these products. Since the late 1940s, the number of cases of insecticide resistance, and the number of species and compounds involved has been continually increasing (Figs. 1 and 2). The 1960s and 1970s saw the appearance of resistance to herbicides and fungicides (Fig. 2). However, the cases of insecticide resistance continue to far exceed the number of cases of herbicide and fungicide resistance (Fig. 2).

In light of its importance, approaches to studying insecticide resistance and insecticide resistance management (IRM) have been widely discussed (e.g. [6–14]). The crop protection industry has long recognized the importance of, and need for effective, proactive resistance management [15–22]. The time, effort, and increasingly very large costs involved in the discovery and development of new insecticides [23] dictate that the chances for the development of resistance be minimized as much as possible to ensure that the very substantial investment made to bring any new insecticide product or trait to the market is not wasted. Likewise, it is equally important to ensure minimize the chances of resistance developing for existing products, since in many instances alternative compounds that possess the same attributes or low cost may not be available. Thus, resistance management is of utmost importance and continues to be a critical concern for all stakeholders involved in modern applied pest control.

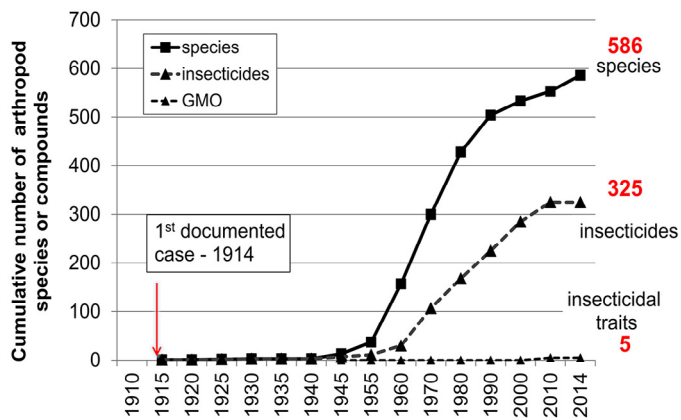
**Abbreviations:** AChE, acetylcholinesterase; APRD, Arthropod Pest Resistance Database; Bt, *Bacillus thuringiensis*; CC, chloride channel; CSI, chitin synthesis inhibitor; EcR, ecdysone receptor; GGCC, GABA gated chloride channel; GMO, genetically modified organism; IRAC, Insecticide Resistance Action Committee; IPM, Integrated Pest Management; IRM, Insecticide Resistance Management; JH-R, juvenile hormone receptor; MET, mitochondrial electron transport; MoA, mode of action; nAChR, nicotinic acetylcholine receptor; NTX, nereistoxin analogs; OA-R, octopamine receptor; Ox-Ph, oxidative phosphorylation; RNAi, RNA interference; Ry-R, ryanodine receptor; VGSC, voltage gated sodium channel; WG, working group; UN, unknown or uncertain mode of action.

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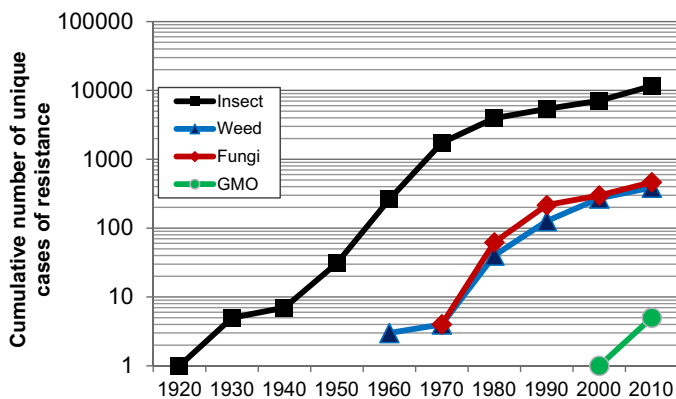
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<http://dx.doi.org/10.1016/j.pestbp.2014.11.014>

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**Fig. 1.** Cumulative increase in (a) the number of species resistant to one or more insecticides, (b) number of insecticides for which one or more species has shown resistance, and (c) number of GMO traits for which resistance has been reported. Data adapted from: [2,3,47–50] and David Mota-Sanchez, Michigan State University, personal communication, 2014.



**Fig. 2.** Cumulative increase in the number of individual cases of resistance for insecticides, herbicides and fungicides. Herbicides and fungicide data adapted from [51,52]. Insecticide data kindly provided by Drs. David Mota-Sanchez, and Mark Whalon, Michigan State University.

## 2. Insecticide Resistance Action Committee (IRAC)

One response to the need for improved resistance management by the crop protection industry was first the formation of the Pyrethroid Efficacy Group and later on the Insecticide Resistance Action Committee (IRAC) [15,16,18,19,21,22] in 1984. IRAC, part of CropLife International, is a technical working group that focuses on providing a coordinated effort by the crop protection industry to prevent or delay the development of resistance in insect, mite and tick pests [22]. The mission of IRAC is twofold: (a) facilitate communication and education on insecticide and trait resistance, and (b) promote the development and facilitate the implementation of insecticide resistance management strategies to maintain efficacy and support sustainable agriculture and improved public health [1,22].

### 2.1. IRAC mode of action (MoA) classification

One of the key tools from IRAC is the MoA Classification Scheme. The MoA Classification Scheme provides state and government agencies, consultants, advisors, growers, universities and extension staff with guidelines for the selection of insecticides and acaricides when used in an alternation or rotation-based resistance management program (see below). Included in the MoA Classification is background information on resistance management and how the MoA Classification can be used for IRM. The MoA classification scheme is available in different formats such as posters (different language versions), a mini booklet and a smartphone App which are regularly updated (Fig 3).

The MoA Classification scheme is based on the best available evidence for the target-sites or MoA of currently available insecticides and acaricides (currently excludes nematicides). Details of the listing have been reviewed and approved by internationally recognized academic and industrial experts in insecticide toxicology, resistance and MoA. Currently the MoA Classification encompasses more than 25 different MoAs. A condensed listing of the chemistries currently covered by the MoA Classification is presented in Table 1; a more comprehensive listing is available on the IRAC website (<http://www.irac-online.org/>). In addition to data from the IRAC MoA classification scheme (main group and primary site of action, chemical subgroup/exemplifying active), Table 1 also provides additional information on the total number of compounds in each group/subgroup, the year the first compound in the group was introduced, and the 2013 end-user market value [24] for that group or subgroup.



**Fig. 3.** Different formats of the MoA classification scheme available on the IRAC website include posters, a mini-booklet and a smartphone App (displayed with permission of IRAC).

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