AFPP – 11th INTERNATIONAL CONFERENCE ON PESTS IN AGRICULTURE
MONTPELLIER – 25th AND 26th OF OCTOBER 2017

MANAGING NEONICOTINOID TARGET SITE RESISTANT *MYZUS PERSICAE* (SULZER) INFESTATIONS IN STONE FRUIT ORCHARDS BY ISOCLAST™ ACTIVE

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ABSTRACT

Isoclast™ active (sulfoxaflor; chemical group sulfoximines) discovered by and proprietary to Dow AgroSciences, is an innovative, new generation insecticide to allow control of critical sap-feeding insect pests in key crops such as tree fruits, vegetables, citrus, potatoes, oilseed rape and cereals. Isoclast exhibits a high degree of efficacy against a wide range of sap-feeding insects, including aphids, whiteflies and scales, many of which are resistant to existing insecticides. The active substances Isoclast and imidacloprid (chemical group neonicotinoids) were tested in 17 open-field trials to assess the susceptibility of field populations of *Myzus persicae* exhibiting the target site R81T mutation which is involved in the resistance to neonicotinoids. Isoclast applied at the proposed registration rate (36 g a.s./ha) efficiently controlled *M. persicae* populations showing the R81T target site mutation in all 17 field trials while imidacloprid could not consistenty deliver reliable aphid control. As these trials clearly show, there was no practical resistance to Isoclast in the tested neonicotinoid resistant *M. persicae* field populations, making Isoclast an excellent foundational insecticide to be utilized against *M. persicae* in insecticide resistance management (IRM) spray programs replacing neonicotinoids.

Keywords: Isoclast; green peach aphid; *Myzus persicae;* efficacy; resistance; sulfoximines; neonicotinoids.

RESUMÉ

INTÉRÊT DE LA SUBSTANCE ACTIVE ISOCLAST™ (SULFOXAFLOR) POUR LUTTER CONTRE LES POPULATIONS DE *MYZUS PERSICAE* (SULZER) PORTEUSES DE LA RESISTANCE DE CIBLE AUX NÉONICOTINOÏDES EN VERGERS DE FRUITS A NOYAUX

La substance active Isoclast™ (sulfoxaflor, famille chimique : sulfoximines) découverte par et proprieté de Dow AgroSciences, est un insecticide innovant destiné à lutter contre les principaux insectes piqueurs-suceurs s'alimentant de la sève des cultures fruitières, légumières, agrumes, pomme de terre, colza et céréales. Elle démontre un haut niveau d'efficacité vis-à-vis d'une gamme étendue de ces insectes tels que les pucerons, les aleurodes et les cochenilles, pour lesquels des résistances aux insecticides sont avérées. Les substances actives Isoclast et imidaclopride (famille chimique : néonicotinoïdes) ont été testées dans 17 essais de plein champ pour évaluer la sensibilité de populations naturelles de *Myzus persicae* présentant la mutation de cible R81T impliquée dans la résistance aux néonicotinoïdes. Appliqué à la dose proposée pour son homologation (36 g s.a/ha), Isoclast, contrairement à l'imidaclopride, permet de contrôler les populations de *M. persicae*. Ces essais en situation de résistance au champ de *M. persicae* aux néonicotinoïdes démontrent l'efficacité d'Isoclast en pratique et permettent d'envisager cette substance active comme une alternative dans les programmes de lutte contre *M. persicae* afin de gérer la résistance des pucerons et notamment contre des populations résistantes aux néonicotinoïdes.

Mots-clés: Isoclast; puceron vert du pêcher; *Myzus persicae*; efficacité; résistance; sulfoximines; néonicotinoïdes.

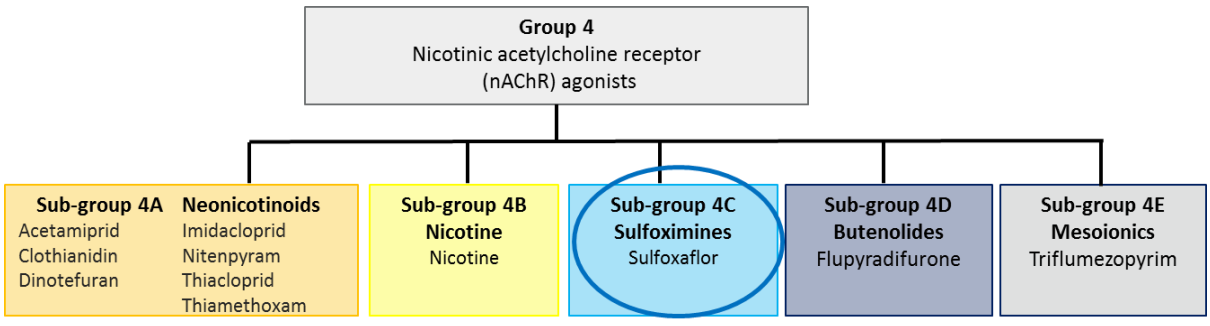
INTRODUCTION

One of the most problematic agricultural pest in the world is *Myzus persicae* (Sulzer) (Hemiptera: Aphididae), known as the green peach aphid. This pest can cause severe damage by both direct feeding and by transmitting more than a hundred plant viruses to many crops (Blackman and Eastop, 2000).
As a result of the intensive use of insecticides, many aphid species, such as *M. persicae*, have developed resistance to products from a range of insecticide chemical classes (Bass *et al.*, 2014). As with other insecticides, the widespread use of neonicotinoids (NNI), such as imidacloprid, has been accompanied with the development of resistance in insect populations, with the first documented report coming less than 6 years after the introduction of imidacloprid (Cahill *et al.*, 1996). There are 2 major resistance mechanism described which are responsible for *M. persicae* loss of susceptibility to imidacloprid (Bass *et al.*, 2015). One of these is based on enhanced detoxification by cytochrome P450s, and the other one is associated with a target site mutation (R81T) in the nicotinic acetylcholine receptor (Bass *et al.*, 2014). The neonicotinoid-resistant populations of *M. persicae* are expanding mainly in stone fruit orchards grown in southern France and across Spain Italy and Greece. This resistance issue causes many problems for farmers who are no longer able to effectively control the *M. persicae* with neonicotinoid compounds, mainly imidacloprid and acetamiprid.
Isoclast™ active is the brand name of sulfoxaflor, which active was discovered by and proprietary to Dow AgroSciences, is an innovative, new generation insecticide to help farmers control critical sap-feeding insect pests in key crops such as tree fruits, vegetables, citrus, potatoes, oilseed rape and cereals. It exhibits a high degree of efficacy against a wide range of sap-feeding insects, including aphids, whiteflies and scales, many of which are resistant to existing insecticides (Sparks *et al.* 2017).

Isoclast belongs to a new and totally different class of insecticide chemistry, known as the sulfoximines. Like some other insecticidal chemistries (including nicotine, neonicotinoids, spinosyns, nereistoxin analogs and butenolides), Isoclast acts on insect nicotinic acetylcholine receptors (nAChRs) (Watson *et al.*, 2011; Sparks *et al.*, 2015). However, the interaction of Isoclast with insect nAChRs is distinct from that of the neonicotinoids and the other, above mentioned, nAChR acting insecticides (Watson *et al.*, 2011 ; Oliveira *et al.*, 2011 ; Wang *et al.,* 2016). The significant structural differences of the sulfxoximines provide unique interactions at the target site and drive significantly different environmental properties. These differences are recognized by the responsible body for insecticide mode of action classifications (Insecticide Resistance Action Committee-IRAC) and as a result IRAC has placed the sulfoximines in a seperate mode of action sub-group 4C (Figure 1).

Figure 1: The IRAC Group 4 insecticides by subgroups.

(Sous-groupes pour les insecticides du Groupe 4 selon le classement IRAC)



The over-expression of the P450 monooxygenase is associated with resistance to many insecticides, including neonicotinoids. However, Isoclast is not metabolized by the P450 monooxygenase enzymes. This

is the main reason why there is no cross-resistance in populations of *Myzus persicae* (green peach aphid) and *Bemisia tabaci* (whitefly), which are resistant to multiple insecticides (Longhurst *et al*., 2012).
The other major type of resistance to neonicotinoids is target site resistance, currently found only in *Myzus persicae* and *Aphis gossypii* (Bass *et al*., 2011; Koo *et al.*, 2014). This resistance has been associated with a point mutation (R81T) in the β1 subunit of the nAChR typically conferring a high level of resistance to imidacloprid and varying degrees of resistance to the other neonicotinoids. In neonicotinoid-resistant *M. persicae*, possessing the target site mutation R81T, only a modest level of cross-resistance was attributed to Isoclast in relation to imidacloprid and several other neonicotinoids detected in 2 cloned *M. persicae* populations (Cutler *et al*., 2013 ; Bass *et al*., 2015).

Globally, Isoclast was first approved for use in 2011 in Korea and currently Isoclast is being used in over 40 countries across the Globe. To date, there is no evidence of practical resistance in the field to Isoclast for any insect species. No reports are available on the field performance of Isoclast on *M. persicae* associated with metabolic resistances and/or the point mutation R81T.

The research presented in this paper reports on the results of 17 open-field trial where the performance of Isoclast was intentionally tested for the control of *M. persicae* populations associated with the point mutation R81T in stone fruit orchards. All trials evaluated Isoclast in paralell with widely used standard products such as imidacloprid, flonicamid and spirotetramat.

MATERIAL AND METHODS

Seventeen field trials were conducted between 2012 and 2016 in Spain, France and Italy to study the effect of Isoclast on different *M. persicae* populations in stone fruit orchards (10 trials in peaches and 7 trials in nectarin). In all selected trials, the NNI target site resistance was determined by genomic analysis detecting the R81T mutation. All trials had 4 replicates, randomized in a complete block design with plot sizes ranging from 12 to 60 m^2. Treatments were applied using backpack sprayers (engine or compressed air), calibrated to deliver a spray volume adequate to cover each crop structure (600-1500 L/ha) using conventional nozzles. All trials were conducted by officially recognized testing organizations using Good Experimental Practices (GEP) and followed the appropriate general European Plant Protection Organization (EPPO) standards PP 1/135, PP 1/152, PP 1/181 and the specific EPPO standards PP 1/258 and CEB No. 17. Isoclast was tested at 36 g a.s./ha dose rate and the efficacy was compared to widely used commercial standards like imidacloprid (150 g a.s./ha), flonicamid (75 g a.s./ha) and spirotetramat (150 g a.s./ha). One application was carried out at the crop growth stage of BBCH 70-75 (post-flowering stage) against well-established aphid populations distributed evenly across the plots. Formulated insecticides used in the field trials were: imidacloprid (CONFIDOR 20LS®, Bayer CropScience), flonicamid (TEPPEKI 50WG®, ISK Biosciences Europe) and spirotetramat (MOVENTO 100 SC®, Bayer CropScience). Isoclast was formulated as Closer®/GF-2626 (120 SC, Dow AgroSciences).

Assessments considered the number of alive aphids per leaf or shoot at different timings according to EPPO standards PP 1/21, PP 1/258 and CEB No. 17. The aphids were counted just before application on samples of 10-50 shoots, with populations of 10 to 1200 aphids per shoot recorded. The same areas of the plants were counted at different dates after application: for knock down (KD) effect at 1-4 days and for residual effect at 6-9, 13-15 and 21-23 days after application (DAA). The efficacy or % Control for each treatment was then calculated using the Henderson-Tilton formula:

$$\%Control = \left(1 - \frac{nTreated_a \times nUntreated_b}{nUntreated_a \times nTreated_b}\right) \times 100$$

or eventually the Abbott formula when the pest distribution was very even before the applications:

$$\%Control = \left(1 - \frac{nTreated}{nUntreated}\right) \times 100$$

where $\mathrm{nTreated_a}$ is the number of insects in the treated plots after the treatment; $\mathrm{nUntreated_b}$is the number of insects in the untreated plots before the insecticide application; $\mathrm{nUntreated_a}$ is the number of insects in the untreated plots after the application and $\mathrm{nTreated_b}$ is the number of insects in the treated plots before the application. The use of the correction with the untreated is an option recommended in trial series analysis when the magnitude of the response variable in the untreated varies greatly from trial to trial (Madden and Paul, 2011).

At each evaluation time, Percent (%) control values were analyzed with a linear mixed model for trial series: $\%\ \mathrm{Control_{ijk}} = \mu + \mathrm{Treatment_i} + \mathrm{Trial_j} + \mathrm{Treatment} \times \mathrm{Trial_{ij}} + \mathrm{Block_{k(j)}} + \mathrm{e_{ijk}}$ with observations normally distributed: Treatment is modeled as fixed effect and the rest of the factors are modelled as random effects (Stroup, 2012). Linear mixed model assumptions (normality and homogeneity of variance) were evaluated with graphical inspection of the residuals. Significance of the fixed effect (Treatment) was evaluated with F-approximate test (α=0.05). The estimation method was restricted maximum likelihood (REML) and Kenward Rodgers for degrees of freedom. Treatment means were compared with Tukey's test (P<0.05). The statistical analysis was performed with R packages Lme4 and multcomp on the basis of the individual plot data (R Core Team, 2015).

The R81T mutation was characterized in the *M. persicae* populations from all field efficacy trials. A mixed sample was collected across the plots having at least a hundred individuals representing the site. The aphids were placed to 70% (V/V) ethyl-alcohol solution and sent to the CBGP-UPM-INIA laboratory in Madrid, Spain for managing the genomic analysis. Twenty-five aphids from each field sample were homogenized, and their genomic DNA was extracted using the protocol described by Bizzaro *et al.* (1996). Isolated DNA concentration was quantified by nanodrop (concentrations were between 0.5 and 2 µg/µL). 500 ng of genomic DNA were used to amplify the DNA fragment containing the putative mutation linked to aphid resistance/susceptibility to neonicotinoid insecticides. For the PCR assay, the CG-Rich polymerase was used and the conditions previously optimized. Because of the amplicon size (142 bp), 3% agarose gel and orange G loading buffer were needed to visualize the amplified DNA bands.

RESULTS

Seventeen field trials were established to evaluate the efficacy of Isoclast against naturally occurring field populations of *M. persicae* in peach and nectarin orchards. Molecular analysis, PCR amplification and sequence analysis of the R81T mutation site in the genomic DNA of the tested *M. persicae* populations detected the resistant genotype in each population used for this article. As pooled samples were used, no information is available on the frequence of the R81T mutation in the populations but the presence of the mutation was confirmed in each sample.

Table I shows the efficacy results and the statistical analysis across the trials.

Efficacy of imidacloprid:

In our 17 field trials where the R81T mutation was detected in the M. persicae populations, the pooled trial average efficacy of imidacloprid was between 51 and 74 % with single locations ranging from 11 to 97 % control during the 3 weeks evaluation period. Only two trials out of the 17 showed imidacloprid delivering more than 90 % efficacy at least one time during the evaluation period. The imidacloprid performance was below the farmers' expectations and also below the average efficacy of the other treatments. In most locations imidacloprid failed to provide any meaningful efficacy.

Efficacy of Isoclast compared to standards (flonicamid and spirotetramat):

Across those same locations, Isoclast delivered sufficient aphid control spanning the entire 3 weeks evaluation period (73-94 % efficacy) being similar or more efficacious than spirotetramat (41-91 %) and

flonicamid (56-88 %). Spirotetramat and flonicamid delivered low knock down activity but their residual efficacy increased and spirotetramat exceeded 90% control by 2 and 3 weeks after the applications. The efficacy of flonicamid dropped below 70 % by the 3rd week after application but still was significantly better than imidacloprid. Spirotetramat and flonicamid are widely used standard aphicides in stone fruit orchards and considered still effective although their slow initial effect noted by the farmers.

Table I : Efficacy of Isoclast in comparison to imidacloprid, spirotetramat and flonicamid against neonicotinoid target site resistant *M. persicae* populations tested in peach and nectarin orchards.

(Efficacité d'Isoclast en comparaison avec celle d'imidacloprid, spirotetramat et flonicamid vis-à-vis de populations de *M. persicae* porteuses de la résistance de cible aux néonicotinoïdes en vergers de pêche et nectarine)

1-4 DAA (1)						
Treatments@ Rate (g a.s./ha)	**Number of trials**	**Efficacy mean (%)**	**Min.**	**Max.**	**std_ error**	**Letters**
Isoclast@36	17	72.9	41.5	96.7	2.7	C
imidacloprid@150	17	66.5	17.1	96.4	3.4	BC
spirotetramat@150	17	40.6	4.3	74.6	3.5	A
flonicamid@70	14	56.0	14.8	92.2	4.0	B
6-9 DAA						
Treatments@ Rate (g a.s./ha)	**Number of trials**	**Efficacy mean (%)**	**Min.**	**Max.**	**std_ error**	**Letters**
Isoclast@36	17	91.3	75.2	99.5	1.3	B
imidacloprid@150	17	74.0	19.5	97.4	3.3	A
spirotetramat@150	17	80.8	43.8	98.7	2.3	AB
flonicamid@70	14	87.5	60.0	99.9	2.0	B
13-15 DAA						
Treatments@ Rate (g a.s./ha)	**Number of trials**	**Efficacy mean (%)**	**Min.**	**Max.**	**std_ error**	**Letters**
Isoclast@36	17	93.6	76.8	100.0	1.3	B
imidacloprid@150	17	66.8	19.8	90.9	3.4	A
spirotetramat@150	17	91.4	56.2	100.0	1.8	B
flonicamid@70	14	85.4	51.7	99.8	2.4	B
21-23 DAA						
Treatments@ Rate (g a.s./ha)	**Number of trials**	**Efficacy mean (%)**	**Min.**	**Max.**	**std_ error**	**Letters**
Isoclast@36	14	84.4	61.2	99.9	2.8	BC
imidacloprid@150	14	51.0	10.9	91.4	4.3	A
spirotetramat@150	14	90.6	64.3	100.0	2.1	C
flonicamid@70	11	68.8	22.0	100.0	4.4	B

(1) DAA: days after application

DISCUSSION

Our field trial results confirmed the farmer claims that there are several areas in the main peach growing areas in Southern Europe where imidacloprid lost its earlier reliable efficacy against *M. persicae*.

Bass *et al*. (2015) revealed that many resistance mechanisms can occur together. In their tested E03-10 C2 clone derived from a field sample from Spain, a range of resistance to several Group 4 insecticides was shown, the resistance factors (RF) were between 70 and 1140 depending on the tested actives. High resistance to deltametrin and pirimicarb (RF: 100+) and medium resistance to pymetrozine (RF: 36) showed that only flonicamid and spirotetramat had no resistance in comparison to the susceptible strain. Isoclast was the least affected among the tested Group 4 insecticides showing the LC90 around the field rate, which suggest a good control of Isoclast in real field conditions.

Wang *et al*. (2016) investigated the interaction of imidacloprid and Isoclast with their target site, on susceptible and R81T resistant *M. persicae*. Their findings showed that both compounds interact with the arginine at position 81 of the green peach aphids β1 subunit of the nACHR but the strenght of binding was deemed much lower for Isoclast than for imidacloprid providing the basis for the reduced effect of this mutation to Isoclast.

In our own laboratory bioassays where we have tested the susceptibility of several neonicotinoid resistant *M. persicae* field populations to imidacloprid and Isoclast, we have not found cross resistance between the 2 compounds (unpublished data). In addition, our 17 field trials presented in this paper also showed that Isoclast provided the best knock down and had numerically similar or better residual control than spirotetramat and flonicamid while imidacloprid failed to provide knock down or residual control of the tested *M. persicae* populations. Thus our studies support the findings by Wang *et al*. (2016) and provide additional evidence that no practical field resistance to Isoclast is associated to date with the presence of the R81T mutation in NNI resistant *M. persicae*.

Kayser *et al.* (2016) revealed that there is likely no single conserved site or mode of binding of neonicotinoids and related nicotinic ligands to their target receptor, but a variety of binding pockets depending on the combination of receptor subunits, the receptor subtype, its functional state, as well as the structural flexibility of both the binding pockets and the ligands. All these observations suggest that there might be significant differences in the “mode of action” of the different compounds belonging to the same IRAC mode of action (MOA) group further highlighting the importance of the existing MOA subgroups in the resistance risk management practices.

As part of the resistance management program, IRAC recommends a rotation of different mode of action insecticides (different IRAC group insecticides) or if no other options are avaialble, secondarily use of subgroups which do not show cross resistance on the field for the management of NNI-resistant *M. persicae*. Options for this IRAC recommended aproach include flonicamid (IRAC group 29), spirotetramat (IRAC group 23) and Isoclast (IRAC group 4C). The results described in this paper supports their use as effective tools that farmers can rely on to manage current resistance issues in *M. persicae*.

CONCLUSION

Isoclast applied at the proposed registration rate (36 g a.s./ha) efficiently controlled *M. persicae* populations showing the R81T target site mutation in seventeen field trials while imidacloprid could not consistenty deliver reliable aphid control. As these trials clearly show, there was no practical resistance to Isoclast in the tested NNI resistant *M. persicae* field populations, making Isoclast an excellent foundational insecticide to be utilized against *M. persicae* in insecticide resistance management (IRM) spray programs replacing neonicotinoids.

ACKNOWLEDGEMENT

The authors would like to thank the following scientists for their assistance in conducting the genomic analysis or the field experiments or doing statistical support and useful comments and discussion: Isabelle Diaz, James Hasler, Pablo Valverde, Enzo Tescari, Rosa Ferrer, Salvador Carrasco, Borja Clemente, Christian Richard, Tom Sparks, Jon Babcock

REFERENCES

Bass C, Puinean A, Andrews M, Cutler P, Daniels M, Elias J, Paul VL, Crossthwaite A, Denholm I, Field L, Foster S, Lind R, Williamson M, Slater R, Mutation of a nicotinic acetylcholine receptor β subunit is associated with resistance to neonicotinoid insecticides in the aphid *Myzus persicae*, BMC *Neurosci*., 12:51, 11p. (2011).

Bass C, Puinean AM, Zimmer CT, Denholm I, Field LM, Foster SP et al., The evolution of insecticide resistance in the peach potato aphid, *Myzus persicae*. *Insect Biochem Mol Biol* 51:41 –51 (2014).

Bass C, Denholm I, Williamson M, Nauen R, The global status of insect resistance to neonicotinoid insecticides: *Pesticide Biochemistry and Physiology* 121: 78–87 (2015)

Bizarro D, Manicardi GC and Bianchi U, Chromosomal localization of a highly repeated EcoRI DNA fragment in Megoura viciae (Homoptera, Aphidiidae) by Nick translation and fluorescence in situ hybridiza¬tion. *Chromosome Res* 4:392–396 (1996).

Blackman RL and Eastop VF, Aphids on the World's Crops, an Identification and Information Guide. John Wiley & Sons Ltd, Chichester, UK, 476 pp. (2000)

Cahill M, Gorman K, Day S, Denholm I, Elbert A and Nauen R, Baseline determination and detection of resistance to imidacloprid in *Bemisia tabaci* (Homoptera: Aleyrodidae). *Bull Entomol Res* 86:343–349 (1996)

Cutler P, Slater R, Edmunds AJF, Maienfisch P, Hall RG, Earley FGP, Pitterna T, Pal S, Paul V-L, Goodchild J, Blacker M, Crossthwaite AJ, Investigating the mode of action of sulfoxaflor: a fourth generation neonicotinoid, *Pest Manag. Sci.* 69:607-619 (2013)

Garzo E, Moreno A, Hernando S, Mariño V, Torne M, Santamaria E, Díaz I, Fereres A, Electrical penetration graph technique as a tool to monitor the early stages of aphid resistance to insecticides. *Pest Manag. Sci*. 72:707-718 (2016).

Hartmut Kayser, Katrin Lehmann, Marilyne Gomes, Wolfgang Schleicher, Karin Dotzauer, Margarethe Moron and Peter Maienfisch, Binding of imidacloprid, thiamethoxam and N-desmethylthiamethoxam to nicotinic receptors of *Myzus persicae*: pharmacological profiling using neonicotinoids, natural agonists and antagonists. *Pest Manag. Sci*. 72:2166-2175 (2016)

Koo H-N, An J-J, Park S-E, Kim J-I, Kim G-H, Regional susceptibilities to 12 insecticides of melon and cotton aphid, *Aphis gossypii* (Hemiptera: Aphididae) and point mutation associated with imidacloprid resistance, *Crop Protect*. 55: 91-97 (2014)

Longhurst, C. L., J. M. Babcock, I. Denholm, K. Gorman, J. D. Thomas, and T. C. Sparks. 2012. Cross-resistance relationships of the sulfoximine insecticide sulfoxaflor with neonicotinoid and other insecticides in the whiteflies *Bemisia tabaci* and *Trialeurodes vaporariorum*. *Pest Management Science* 69: 809–813.

Madden LV and Paul PA, 2011. Meta-analysis for evidence synthesis in plant pathology: An overview. *Phytopathology* 101:16-30.

Oliveira EE, Schleicher S, Buchges A, Schmidt J, Kloppenburg P, Salgado VL, Desensitization of nicotinic acetylcholine receptors in central nervous system of the stick insect (*Carausius morosus*) by imidacloprid and sulfoximine insecticides, *Insect Biochem. Molec. Biol*. 41:872-880 (2011)

R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria., URL *http://www.R-project.org/*

Stroup, WW 2012. Generalized linear mixed models: Modern concepts, methods and applications. CRC press, Boca Raton, FL
Sparks TC, Nauen R, IRAC: Mode of action classification and insecticide resistance management, *Pestic. Biochem. Physiol*. 121:122-128 (2015).

Sparks TC, Loso MR, Watson GB, Wang NX, Buysse AM, Nugent, BM, Kramer V, Gomez LE, 2017, Sulfoximine Insecticides: Sulfoxaflor, In *Modern Crop Protection Compounds*. Vol. 3, 3nd ed. (P. Jeschke, M. Witschel,, W. Kramer, U. Schrimer, eds.), Wiley-VCH, New York, In press.

Wang N, Watson G.B, Loso m.R, Sparks T.C, Molecular Modeling of Sulfoxaflor and Neonicotinoid Binding in Insect Nicotinic Acetylcholine Receptors: Impact of the *Myzus* β1 R81T Mutation. *Pest Manag. Sci.* 69:607-619 (2016)

Watson GB, Loso MR, Babcock JM, Hasler JM, Letherer TJ, Young CD, Zhu Y, Casida JE, Sparks TC, Novel nicotinic action of the sulfoximine insecticide sulfoxaflor, *Insect Biochem. Mol. Biol*., 41:432-439 (2011)