

**GOALS, ACHIEVEMENTS AND FUTURE  
CHALLENGES OF THE ARIZONA WHITEFLY  
RESISTANCE MANAGEMENT PROGRAM**

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**Abstract**

A whitefly resistance crisis in Arizona in 1995 prompted the development of a resistance management strategy in 1996 that recommended maximal once per season use of each of two insect growth regulators, Knack® (pyriproxyfen) and Applaud® (buprofezin), and limited and delayed use of synergized pyrethroid insecticides in cotton. Implementation of this strategy has substantially reduced the numbers of insecticide applications made to control whiteflies, and statewide monitoring has shown increased whitefly susceptibility to synergized pyrethroids and key non-pyrethroid insecticides. Having benefited from two years of success with this strategy, the Arizona cotton industry now faces the question of whether it can be sustained as Knack and Applaud gain additional registrations for use against whiteflies in vegetables, melons and glasshouse crops. Integrally linked to the current success of whitefly control in Arizona is use of the chloronicotinyl insecticide, Admire® (imidacloprid) as a systemic treatment in vegetables and melons. Plans to register additional chloronicotinyl compounds for use in cotton raise concerns, especially in light of reports of whitefly resistance to imidacloprid in Europe and findings that Arizona whiteflies have become progressively less susceptible to imidacloprid in each of the past two years. Within the context of these new insights we suggest specific actions intended to sustain the current success of whitefly management in Arizona cotton. These involve continued emphasis on limiting the use of IGRs and chloronicotinyl compounds and harmonizing new registrations of these compounds to manage whitefly resistance on an ecosystem, rather than crop-specific basis.

**Introduction**

Since the late 1980's, whiteflies have caused severe damage to cotton, vegetable, and melon crops grown in the irrigated deserts of the southwestern US (Byrne et al. 1990). In

cotton, whitefly densities exceeding 5-10 adults per leaf can result in severe reductions in lint quality due to stickiness caused by excreta (honeydew) and subsequent development of sooty mold fungi (Diehl and Ellsworth 1995). Intensive reliance on a limited array of insecticides to combat whitefly populations resulted in an insecticide resistance crisis in Arizona cotton in 1995. This crisis prompted the formulation and implementation of a whitefly resistance management program detailed by Dennehy and Williams (1997).

Implementation of the Arizona whitefly resistance management program represented a significant achievement for Arizona cotton. As well as outlining its background and achievements over the past two seasons, this paper is intended to highlight the fragility of the current success and the dangers ahead as the insect growth regulators (IGRs), Knack® (pyriproxyfen) and Applaud® (buprofezin) gain additional registrations for use against whiteflies in vegetables, melons and glasshouse crops and as new chloronicotinyl insecticides are promoted for use in cotton. Avoiding a return to the treadmill of uncontrollable resistance and ineffective insecticide applications for whitefly control will require unprecedented cross-commodity and public and private sector cooperation to harmonize insecticide use in the cotton, vegetable melon agro-ecosystem in Arizona.

The whitefly resistance management program for Arizona cotton (Dennehy et al. 1996a), first implemented in 1996, was formulated and implemented under the aegis of the Southwest Whitefly Resistance Working Group. This group represented a collaboration involving Cotton Incorporated, the Arizona Cotton Growers Association, Federal and State pest managers, The Environmental Protection Agency and two Chemical producers, AgrEvo USA Company and Valent USA Corporation.

Whitefly susceptibility to insecticides was monitored on a statewide basis since 1994 by the Extension Arthropod Resistance Management Laboratory (EARML). This provided early warning (Dennehy et al. 1995) of the onset of severe whitefly resistance to the so-called synergized pyrethroid insecticides--predominantly Danitol® (fenpropathrin) mixed with Orthene® (acephate). By the end of the 1995 season, producers in problem areas were experiencing failure of essentially all insecticides registered for whitefly control. Some cotton growers were resorting to very expensive mixtures of three and four insecticides and, even after having made 8-12 insecticide applications, experienced unacceptably high whitefly densities (Dennehy and Williams 1997). From these observations in 1995 it was clear that major changes had to be made to avert a financial crisis for cotton producers in the coming season.

## **Goals and Design of the Program**

The proposed solution to the whitefly resistance crisis of 1995 was modeled after a successful resistance management program implemented in Israel (Horowitz et al. 1994) that was centered around strategic use against whiteflies of the insect growth regulators (IGRs) buprofezin (Applaud<sup>®</sup>) and pyriproxyfen (Knack<sup>®</sup>). The Israeli and Arizona programs had in common the following fundamental goals: 1) conserving natural enemies, 2) limiting insecticide use, and 3) diversifying the insecticides used against whiteflies in cotton. Based on the resistance management rationale of diversifying the insecticide use regime, approval was requested and subsequently obtained from EPA for emergency (Section 18) exemptions for two IGRs. Significantly, the exemptions restricted use of both compounds to once each per season.

Whitefly insecticide use was recommended to follow three stages. The first comprised use of IGRs when whiteflies exceeded thresholds (Stage I), followed by use of non-pyrethroid conventional insecticides (Stage II), and lastly, when necessary, use of no more than 2 applications of synergized pyrethroid insecticides (Stage III). This placed greatest emphasis early in the season on the highly effective new IGRs and conserved natural enemies by delaying use of pyrethroid insecticides for as long into the growing season as possible. Regulatory restrictions limiting the IGRs to once per season coupled with the three stages of the strategy increased the likelihood that growers would avoid over-reliance on the IGRs and would diversify the insecticides used from other cross-resistance groups. These measures were coupled with renewed emphasis on whitefly monitoring, thresholds (Ellsworth et al. 1996) and cultural control methods to comprise the complete integrated resistance management strategy. Further details of the program can be found in Dennehy et al. (1996a).

## **Achievements**

Success of the Arizona whitefly resistance management program is being measured in the short-term by the degree to which growers have experienced improved whitefly control in the field and the correlate, per-acre numbers of whitefly treatments per season. The longer-term and more objective evaluation of success comes from resistance monitoring throughout the State. If the resistance management program is completely successful it will allow susceptibility of populations to be regained to the entire suite of whitefly insecticides but especially to the synergized pyrethroids. Also, it is our hope that limiting use to once-per-season for each IGR will prevent reductions in susceptibility to these insecticides.

## **Control Observed in the Field**

In 1996, both grower experiences and large-scale demonstration trials (see citations in Dennehy and Williams

1997) reported excellent whitefly control at locations employing the resistance management strategy. In areas such as Gila Bend, where we documented the highest levels of pyrethroid resistance in 1995, many of the fields that received 8-12 whitefly treatments in 1995 required only 1-4 insecticide applications in 1996 (Dennehy and Williams 1997). This trend was sustained in the 1997 season. Statewide averages for season-long numbers of whitefly treatments per cotton field were estimated to have been reduced from 6.6 in 1995 to 2.0 in 1996 and 1.8 in 1997 (Ellsworth 1998).

## **Monitoring of Whitefly Resistance to Insecticides**

Arizona whiteflies have become significantly more susceptible to synergized pyrethroid insecticides and key non-pyrethroid insecticides in each of the past two year since implementation of the strategy. Methodology used for monitoring whitefly susceptibility was described in Dennehy and Williams (1997). The following summary of results for the 1997 season are detailed in Dennehy et al. (1998). Additional detailed results of yearly monitoring of whitefly susceptibility, beginning in 1994, may be found in Dennehy et al. (1995, 1996b, and 1997).

*Synergized Pyrethroids.* Contrasts of 1995, 1996, and 1997 results from statewide collections show significant increases in overall susceptibility to Danitol+Orthene each of the past two years (Fig. 1). There has been a striking loss of the most highly resistant populations over that time. Median mortality in 1995 was 54% in assays of 10  $\mu\text{g/ml}$  fenpropathrin (Danitol) + 1000  $\mu\text{g/ml}$  acephate (Orthene) and some populations had less than 10% mortality in assays employing this concentration. By 1997 median mortality was 83% and all populations had >40% mortality at this same concentration (Fig. 1).

Sivasupramaniam et al. (1997) showed that resistance to Danitol+Orthene conferred cross-resistance to all of the pyrethroids evaluated for controlling whiteflies in Arizona. Our strategy continues to emphasize holding the synergized pyrethroids in reserve to be used as a last resort, should they be needed late in the season when the crop is at greatest risk of being contaminated by honeydew. These 1996 and 1997 data support the conclusion that the Arizona whitefly resistance management program has yielded benefits in terms of reductions in resistance to synergized pyrethroids.

*Conventional Non-Pyrethroid Insecticides.* Reduced insecticide use resulting from implementation of the resistance management strategy has been associated with increased whitefly susceptibility to some non-pyrethroid insecticides. Susceptibility to Gowan Thiodan<sup>®</sup> (endosulfan) increased numerically throughout the State in 1996 (not statistically significant) and 1997 (statistically significant), relative to 1995 (Fig. 2). Susceptibility of Arizona populations to Ovasyn<sup>®</sup> (amitraz) increased slightly and significantly from 1995 to 1996 but then decreased significantly from 1996 to 1997 (Fig. 3). This may reflect

increased use of Ovasyn in 1997. Ovasyn is an important conventional non-pyrethroid insecticide used singly and in mixtures against whiteflies in Arizona. As such, these results indicate that care must be taken to use this insecticide in rotations of products that will avoid its overuse.

Monitoring revealed no changes in overall susceptibility to the mixtures of Thiodan+Ovasyn and Curacron® (profenofos)+Lorsban® (chlor-pyrifos) from 1996 to 1997. However mean and median responses of populations showed slightly greater susceptibility to mixtures of Curacron+Vydate® (oxamyl) in 1997 than 1996 (Dennehy et al. 1998).

**Insect Growth Regulators.** Results of monitoring of Arizona whitefly susceptibility to buprofezin (Applaud) and pyriproxyfen (Knack) are being analyzed at the time of this writing and will be reported elsewhere. We are aware of no reports of field failures of these IGRs in Arizona in 1997.

**Chloronicotinyl Compounds.** Susceptibility to Admire® (imidacloprid) of whitefly populations collected from cotton has declined significantly each of the past two years (Fig. 4). However, very little of this active ingredient has been applied to cotton (Williams et al. 1998). The reduced susceptibility to Admire results from extensive use of this systemic insecticide in vegetables and melons. Its extreme effectiveness in vegetables and melons has meant reduced movement of whiteflies into cotton during the critical early months of cotton development. For this reason there is an inter-dependence of whitefly control in cotton, vegetables, and melons. Loss of efficacy of Admire in vegetables and melons will translate into serious problems for cotton growers in Arizona.

### **Summary of Achievements.**

Deployment of the whitefly resistance management strategy has coincided with substantially reduced numbers of whitefly treatments per acre in Arizona cotton. Additionally, statewide monitoring over the past two years has shown significantly reduced resistance of Arizona whiteflies to the synergized pyrethroid insecticides. This reflects a major advancement since it was over-reliance on synergized pyrethroids that induced the resistance crisis that culminated in 1995. We have also documented increases in susceptibility to some conventional non-pyrethroid insecticides. However, over each of the past two years we have documented reductions in susceptibility of Arizona whitefly to the chloronicotinyl compound, Admire. Though detected in collections from cotton fields, this change is believed to have resulted from use of this class of materials on vegetables and melons, not cotton.

### **Future Prospects and Challenges**

After two years of implementation, the program is reaching a critical stage in its development. Two factors in particular have the potential to exert a profound influence on its

design and sustainability for the foreseeable future. Firstly, when the two IGRs achieve full registration, restrictions on their use will no longer be obligatory as under the current Section 18 exemption. Secondly, imidacloprid is likely to be supplemented shortly by other, closely related insecticides (e.g. acetamiprid) that will extend the utility and potential use of chloronicotinyl chemistry against *Bemisia*. The implications of these developments need very careful scrutiny, taking full account of information on resistance risks available from elsewhere in the world.

No insecticides are immune from resistance, and already there are examples from elsewhere in the world of resistance to novel compounds that are currently being used in Arizona. Not surprisingly, most of these refer to areas where particular products have been used excessively in contravention of manufacturer's recommendations, and/or where ecological conditions (as in glasshouses) promote rapid selection of genes to economically-damaging frequencies. A 75-fold resistance to the insect growth regulator buprofezin (Applaud in US cotton) was first detected in a *Bemisia* strain collected from ornamental plants in a Dutch glasshouse sprayed 22 times with this chemical over an 18 month period during 1991 and 1992 (Cahill and Denholm, 1993). Subsequent testing has shown buprofezin-resistant individuals to be present at varied frequencies in several Dutch and UK glasshouses, and at generally low frequencies on vegetables in southern Spain and on cotton in Mexico (Cahill et al. 1996a and unpublished data). Horowitz and Ishaaya (1994) also demonstrated *ca.* 12-fold resistance in insects collected from an Israeli greenhouse in 1993. Another primary target of buprofezin is the glasshouse whitefly, *Trialeurodes vaporariorum*, which has been found to exhibit very potent resistance to this chemical in New Zealand (Workman and Martin, 1995) and Europe (De Cock et al. 1995; M. Cahill, pers. comm. 1998).

Resistance to pyriproxyfen (Knack in US cotton) has only been reported to date from Israel. It was first detected in insects collected from a rose greenhouse that had received three successive applications of this compound. Interestingly, resistance factors were much higher when expressed in terms of egg hatch (550-fold at LC<sub>50</sub>) than nymphal and pupal survival (10-fold; Horowitz and Ishaaya, 1994). Alarming, highly-resistant individuals have now also been detected at high frequencies on cotton at certain localities in central and eastern Israel (A.R. Horowitz, pers. comm. 1997), despite pyriproxyfen use on cotton being limited to one application per season. Factor(s) promoting the build-up of pyriproxyfen resistance on Israeli cotton in some sites but not others are still unclear. It is likely, however, that they reflect underlying differences in the ecology of *Bemisia*, in particular the availability of alternative host plants when pyriproxyfen is applied to cotton. Similar differences in whitefly bionomics have been implicated to account for geographical variation in the extent of *Bemisia* resistance to older insecticides in Arizona

cotton (Dennehy et al. 1996b, 1997). As yet nothing is known about the biochemical or physiological basis of resistance to buprofezin or pyriproxyfen, but there is no evidence that the two chemicals can share the same resistance mechanism.

Due to its effectiveness as a seed treatment, soil application and foliar spray imidacloprid is now achieving widespread use against *Bemisia* around the world, and against coexisting pests including aphids and thrips. Its known mode of action, binding to nicotinic acetylcholine receptors in the post-synaptic region of insect nerves (Bai et al. 1991), renders it potentially vulnerable to resistance based on a target-site modification, as well as to enhanced metabolic degradation. Prabhakar et al. (1995) were the first to demonstrate a potential for *Bemisia* to develop resistance to imidacloprid. Intensive selection in the laboratory of a strain collected from imidacloprid-treated melon fields in southern California caused a gradual increase in tolerance to this chemical. After 32 generations, resistance factors had reached c. 80-fold as expressed in a hydroponic bioassay (Prabhakar et al. 1997). Results of laboratory selections should be interpreted with care (e.g. Roush and McKenzie, 1987), but have now been supplemented by data showing *Bemisia* populations on vegetables in southern Spain to contain varying frequencies of insects capable of withstanding very high concentrations of imidacloprid (Cahill et al. 1996b). Over the last three years, whiteflies collected from different localities in Arizona have also exhibited a tendency to survive very high concentrations (Williams et al. 1998) and this has increased significantly from one season to the next (Fig. 4). Mechanism(s) responsible for these increases in tolerance are unclear at present, although biochemical assays have been developed that should assist with identifying possible changes in binding affinity to the primary target site (eg. Chao et al. 1997). At present there are insufficient data to predict how any resistance selected by imidacloprid will affect the efficacy of other chloronicotinyl insecticides. However, the structural similarity of these chemicals, coupled most likely with a common site of action, implies a strong probability of cross-resistance - a threat conceded by the manufacturers of imidacloprid themselves (Elbert et al. 1996).

Collectively, these findings demonstrate that all three novel insecticides in use against *Bemisia* in Arizona present a tangible resistance risk that can only be averted by maintaining strict controls over their use. It is essential that resistance management recommendations for the future continue to be based on the same three principles as before, i.e. making full use of the range of chemicals available to present as diverse a challenge to insects as possible, restricting the use individual products to avoid prolonged selection for specific resistance genes, and coordinating the use of insecticides on different crops to preclude repeated exposure to the same chemicals on a succession of host plants throughout the year. While recognizing the need for recommendations to be discussed and endorsed by all

sectors of the pest management and cotton-growing communities, we propose the following as being both scientifically justified and compatible with retaining control of *Bemisia* in the agro-ecosystems in which it occurs in Arizona:

### **1. Limit and Harmonize IGR Use**

The development of resistance to buprofezin or pyriproxyfen affords possibly the greatest threat of all to the sustainability of the Arizona program. In view of developments in Israel with pyriproxyfen (see above), it is apparent that restricting these to even a single application per season may not preclude the selection of resistance in areas where whiteflies are concentrated on cotton at the time of spraying. Current limitations on IGRs therefore appear fully justified and should be retained following expiration of the Section 18 exemption. Furthermore, these chemicals have established such a key role on cotton that any extension of their use to vegetables at other times of the year should be undertaken with extreme caution, especially in parts of the State where alternative, untreated hosts (e.g., alfalfa) are not sufficiently abundant to moderate resistance build-up by *Bemisia*.

### **2. Limit and Harmonize Chloronicotinyl Use**

At present, imidacloprid is applied primarily to vegetables, where its outstanding systemicity can be exploited to better effect than on cotton. Fortuitously this has led to a *de facto* division of chemistry between crops; chloronicotinyls and IGRs being limited largely to vegetables and cotton respectively. Due to commercial pressures and differences in the physico-chemical properties of chloronicotinyl molecules, it may prove impossible to maintain this state of affairs indefinitely. The next insecticide in this class likely to be introduced to Arizona is acetamiprid, whose contact activity renders it more potent than imidacloprid as a foliar spray against *Bemisia* (A.R. Horowitz, pers. comm. 1997, T.J. Dennehy, unpublished data). Probably the most important of all the resistance management tactics advanced for chloronicotinyls so far is to prevent a succession of systemic and foliar treatments on the same crop (Elbert et al. 1996). Hence the scenario of permitting foliar sprays of acetamiprid to vegetables already treated systemically with imidacloprid or acetamiprid should be avoided at all cost. This in turn is likely to increase commercial pressure to apply foliar treatments of chloronicotinyls on cotton. If so, we very strongly endorse limiting their use on cotton to treatments against early-season sucking pests (*Aphis gossypii* and *Lygus hesperis*) and prohibiting their use specifically against *Bemisia*. Harmonizing the use of chloronicotinyls in this way would have the dual advantages of exploiting their full spectrum of activity while (hopefully) safeguarding the very significant benefits to cotton that stem from maintaining excellent whitefly control in melons and vegetables.

### **3. Diversify Insecticides Used Against Whiteflies**

After using IGRs, if foliar sprays are needed to control *Bemisia* on cotton, growers should resort to conventional chemicals instead of chloronicotinyls. The substantial reduction in insecticide use on cotton in Arizona over the last two years has already prompted a restoration of whitefly susceptibility to synergistic combinations of pyrethroids and organophosphates (see above). If this trend continues there is every prospect that older conventional insecticides will retain a critical role in protecting against over-use of newer products. For this to succeed, however, it is critical that pyrethroids be reserved for late-season use in cotton, when needed at all.

### **4. Intensify Utilization of Whitefly Monitoring and Thresholds**

Adherence to IPM principles and non-chemical control tactics is the backbone of any resistance management program. Aside from recommendations on the use of particular products, continued emphasis on relevant pest monitoring procedures and validated treatment thresholds is vital to minimize overall insecticide inputs and hence the intensity of selection for resistance mechanisms.

### **5. Continue Vigilant Monitoring of Resistance**

Since 1994, statewide monitoring of changes in susceptibility of *Bemisia* and other cotton pests has proved pivotal in supporting the implementation of the resistance management program. It is critical for objectively evaluating the success of the program and for allowing the strategy to be modified to account for unforeseen circumstances. Of particular relevance at the present time is tracking changes in whitefly susceptibility to chloronicotinyl and IGR compounds in glasshouses and vegetable and melon crops since resistance developments in these settings pose a clear threat to the long-term stability of whitefly management in cotton.

### **Conclusions**

Implementation of the Arizona whitefly resistance management program represents a significant achievement for Arizona cotton. After outlining its background and achievements over the past two seasons, we highlighted the fragility of the current success and the dangers ahead as the IGRs gain additional registrations for use against whiteflies in vegetables, melons and glasshouse crops and as new chloronicotinyl insecticides are registered for use in cotton. Avoiding a return to the treadmill of uncontrollable resistance and ineffective insecticide applications for whitefly control will require unprecedented cross-commodity and public and private sector cooperation to harmonize insecticide use in the cotton, vegetable melon agro-ecosystem in Arizona.

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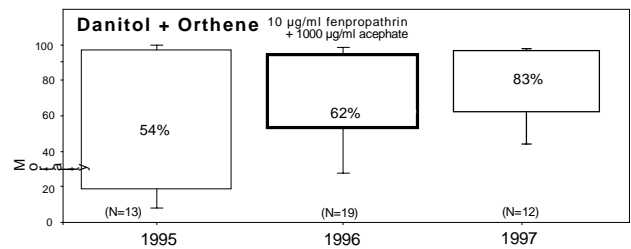


Figure 1. Box plots illustrating the significant increase observed in susceptibility of Arizona whitefly populations to Danitol® (fenprothrin) + Orthene® (acephate) from 1995 through 1997. Note that there has been a progressive loss of the most resistant populations. From Dennehy et al. (1998).

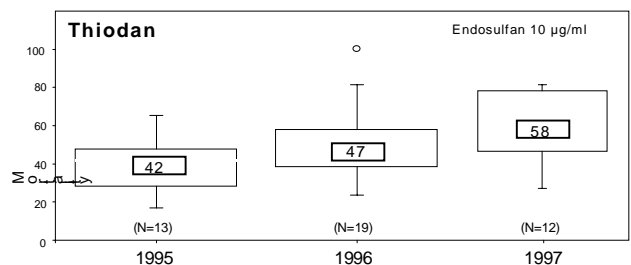


Figure 2. Box plots illustrating the significant increase observed in susceptibility of Arizona whitefly populations to Gowan Thiodan® (endosulfan) from 1995 through 1997. Note that each year there has been a small but significant overall increase in susceptibility of populations from throughout Arizona. From Dennehy et al. (1998).

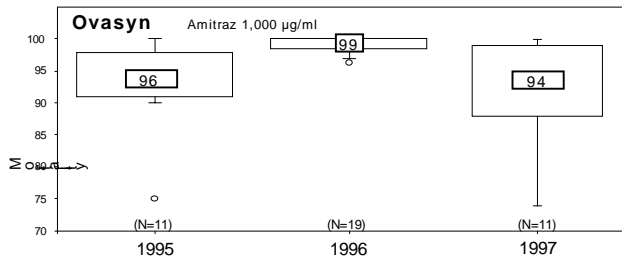


Figure 3. Box plots illustrating the changes in susceptibility of Arizona whiteflies to Ovasyn® (amitraz) from 1995 through 1997. Note that there was a small but significant increase in susceptibility of populations from 1995 to 1996 and a significant reduction in susceptibility to Ovasyn® from 1996 to 1997. From Dennehy et al. (1998).

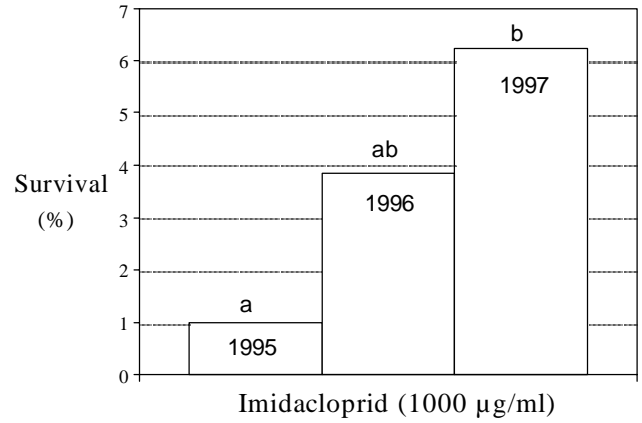


Figure 4. Reduced susceptibility of Arizona whiteflies to imidacloprid (Admire®) from 1995 to 1997. Mean survivorship in bioassays of 1000 µg/ml across all locations has increased each of the past two years in statewide surveys. From Williams et al. (1998).