The Role of the IR-4 Project in the Registration of Plant Growth Regulators in Horticultural Crops

Jerry J. Baron,[1] Robert E. Holm,[2] and J. Ray Frank[3]

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Summary. The pest management industry does not have adequate financial incentives to develop the required data to register pest management tools with government authorities on fruit, vegetables, herbs, spices, nursery crops, landscape plants, flowers, turfgrass, and other specialty crops. Growers of these crops, collectively called minor crops, need pest control tools to be able to sustain production. The Interregional Research Project Number Four (IR-4) was established in 1963 by the U.S. Department of Agriculture to assist growers of minor crops by providing a mechanism to allow growers of these crops to have access to safe and effective pest management tools. Working with research, industrial and extension personnel at the state land-grant institutions and researchers at USDA, Agricultural Research Service, IR-4 develops the appropriate data to support registration of insecticides, fungicides, herbicides and plant growth regulators. Many of the uses of plant growth regulators in current use were developed with oversight provided by IR-4. There are many promising new plant growth regulators and/or uses in the commercial development pipeline and it is anticipated that assistance from IR-4 will be needed to support registration of these new materials on minor crops.

Fruit, vegetables, herbs, spices, nursery crops, landscape plants, flowers, forest trees, turfgrass, interior plants, and other specialty crops are worth over $40 billion per year in domestic sales. This accounts for about 40% of the total annual agricultural sales for the US. In spite of the huge economic importance of these crops, which are collectively called minor crops, there is frequently insufficient financial incentive for the industry to invest the necessary resources in registering plant growth regulators and other crop protection tools for these crops. Development, testing, registration and personnel time are huge expenses for the registrants. To maximize the return on investment, most plant growth regulators and pest control products are targeted where there is potential for large sales. The target markets are usually major acreage crops such as corn (*Zea mays*), soybean (*Glycine max.*), cotton (*Gossypium* sp.), and small grains. Horticultural crops often end up with few plant growth regulators and pest control tools despite their high value and importance.

[1]Assistant Director, IR-4 Project, 681 US Highway 1 South, Cook College, Rutgers University, North Brunswick, NJ 08902; e-mail: jbaron@aesop.rutgers.edu.

[2]Executive Director, IR-4 Project, 681 US Highway 1 South, Cook College, Rutgers University, North Brunswick, NJ 08902; e-mail: holm@aesop.rutgers.edu.

[3]Ornamental Project Manager, IR-4 Project, 6916 Boyers Mill Rd. New Market, MD 21774.

Table 1. Active IR-4 research projects with plant growth regulators on minor food crops.

Crop	Plant growth regulator[z]	Purpose
Almond (*Prunus dulcis*)	NAA	Sucker control
Apple (*Malus domestica*)	Hydrogen cyanamid	Blossom thinner
Blueberry (*Vaccinium* sp.)	Ethephon	Delay spring flowering and prevent frost damage
Blueberry	Hydrogen cyanamid	Blossom thinner
Cherry, sweet (*Prunus avium*)	AVG	Reduce fruit softening and decay
Coffee (*Coffee arabica*)	Ethephon	Promote uniform ripening
Cranberry (*Vaccinium macrocarpon*)	Ethephon	Enhance fruit color development
Fig (*Ficus carica*)	Ethephon	Promote uniform ripening
Filbert (*Corylus* sp.)	Ethephon	Promote earlier harvest
Grapefruit (*Citrus* x *paradisi*)	MBTA-HCl	Increase sugar content
Grapefruit	NAA	Enhance natural abscission
Kiwifruit (*Actinidia deliciosa*)	Hydrogen cyanamid	Blossom thinner
Orange (*Citrus sinensis*)	NAA	Enhance natural abscission
Peach (*Prunus persica*)	Ethephon	Delay spring flowering and prevent frost damage
Peach	Hydrogen cyanamid	Blossom thinner
Peach	AVG	Reduce fruit softening and decay
Pepper (transplants) (*Capsicum* sp.)	Uniconazole	Control height before field planting
Plum (*Prunus domestica*)	AVG	Reduce fruit softening and decay
Plum	Hydrogen cyanamid	Blossom thinner
Plum	NAA	Sucker control
Pomegranate (*Prunus granatum*)	NAA	Sucker control
Potato (*Solanum tuberosum*)	Prohexadione calcium	Reduce vine growth
Strawberry (*Fragaria* ×*ananassa*)	Prohexadione calcium	Reduce runner growth
Tomato (transplants) (*Lycopersicon esculentum*)	Uniconazole	Control height before field planting
Walnut (*Juglans* sp.)	NAA	Sucker control

[z]NAA = 1-naphthaleneacetic acid, AVG = aminoethoxyvinylglycine, MBTA-HCl = diethyl-2-(4-methylbenzyloxy) ethylamine hydrochloride.

To minimize the so-called minor use problem, USDA, the state agriculture experiment stations, and land grant institutions developed a nationwide research program to provide solutions. The program was titled the Interregional Research Project Number Four and is commonly know as the IR-4 Project. This project was first established in 1963 with the objective of developing data for conventional chemical and plant growth regulators to support their regulatory clearance on vegetables, fruit, herbs, and other minor food and fiber crops. Since IR-4's inception, the objectives were expanded in 1977 to include data development to support the regulatory clearance of plant growth regulators and crop protection chemicals on ornamental crops and in the clearance of biopesticides. The IR-4 has evolved to where many feel it is involved in the leading edge of new pest control technologies. However, the project remains a unique publicly funded partnership organization between the USDA's

Table 2. The biological activity for recently developed plant growth regulators.

Plant growth regulator	Trade name[z]	Supplier
Ammonium thiosulfate		Siemer, Germany
Aminoethoxyvinyl-glycine (AVG)	RETAIN	Valent BioScience, Libertyville, Ill.
Bacillus cereus		Microflo, Memphis, Tenn.
Clofencet	DETASSELOR	Monsanto, St. Louis, Mo.
Copper ethylenediamine complex	INFERNO	Griffin, Valdosta, Ga.
Diphenylamine (*N*-phenylbenzenamine)	DPA	Syngenta, Greensboro, N.C.
2,6-Diisopropylnapthalene (2,6-DIPN)	AMPLIFY	United Agriculture Products, Greeley, Colo.
Gamma-aminobutryic acid (GABA)	AUXI GRO	Emerald BioAgriculture, Lansing, Mich.
Gibberelins and N-(phenyl methyl)-H-purine-6-amine	RITE SIZE	Agtrol, Houston, Texas
Diethyl-2-(4-methylbenzyloxy) ethylamine hydrochloride (MBTA-HCl)	ECOLYST	Valent BioScience
1-Methylcyclopropene (1-MCP)	ETHYLBLOC	Biotechnologies for Horticulture, Philadelphia, Pa.
Mmepiquat chloride	PIX	BASF Agriculture Products, Research Triangle Park, N.C.
Phospholipid	LYSO PE	JP Bioregulators, Middleton, Wis.
Prohexadione calcium	APOGEE	BASF Agriculture Products
Sodium nitrophenolate	ATONIC	Asahi Manufacturing Ltd., Japan
Trinexapac-methyl	PALISADE	Syngenta

[z]Trade name indicated in capital letters if available.

Agriculture Research Service (ARS) and Cooperative State Research Education and Extension Service (CSREES) and the land grant university system. The IR-4 is the only publicly funded program that conducts research and submits petitions to US Environmental Protection Agency (EPA) for registration of pest control products. In practical terms, IR-4 serves as the intermediate between the EPA and the registrants to facilitate label expansion of chemical and biological registrations on major crops to minor crops.

IR-4's university research network consists of 19 field research centers, four major analytical laboratories and 6 satellite analytical laboratories. The USDA-ARS network with three annual laboratories and seven-field research centers complements this. The research program is coordinated by the National Headquarters at Cook College, Rutgers University and the regional offices at University of Florida, Gainesville; Michigan State University, East Lansing; New York State Agricultural Experiment Station, Geneva; and University of California, Davis. Each year IR-4 conducts about 120 studies on food crops that consist of 700 field trials, about 500 trials on ornamental and greenhouse crops and about 35 biopesticide projects. For food crops, field trials are established in appropriate geographic areas where the crop is normally grown and specified by the EPA's 13 geographical regions. The scientists apply the test chemical in the manner that was shown to be safe and effective in preliminary product performance experiments. At normal harvest time, the commodity of interest is removed from the plant, quick-frozen and transferred to an analytical laboratory where the concentration of the chemical remaining in the commodity is determined. Nonfood crops and materials that have an exemption from the requirements of a pesticide tolerance only require adequate crop safety and product performance data to ensure the registrant that the proposed new use is safe on the crop and effective in controlling the target pests.

IR-4's success in providing pest management solutions can be measured by the large number of minor crop pest control registrations of a chemical or biological tool on a specific crop established or retained as a result of IR-4's efforts. An IR-4 clearance is defined as a pest control agent and commodity combination that supports a registration. Registration of a specific use is the responsibility of the agrochemical manufacturer, who is the seller of the product. These clearances on food crops, numbering over 5,500 chemicals and 200 biological since 1963, are the direct result of IR-4 research efforts that provide data which supports the establishment of pesticide tolerances or exemption of tolerances by EPA. This quantity is over 40% of the total number of clearances granted by EPA. IR-4 research on ornamental species is equally impressive, over 8,800 clearances since 1977.

Most requests for assistance to IR-4 come from federal and state researchers/extension scientists involved in minor crop pest management. IR-4 also receives requests directly from growers and/or organizations representing a commodity. The only group of IR-4 stakeholders prohibited in submitting requests is representatives of agricultural chemical companies.

A request for assistance consists of the completion and submission of a simple one-page Project Clearance Request (PCR) form. Completed forms can now be submitted electronically via the IR-4's web site, <http://www.cook.rutgers.edu/~ir4> (Baron, 2001). This form seeks some basic information, such as the crop, the proposed pest management tactic, the target pest(s) in question, the proposed use of the pest management tool including the application rate and timing, the interval from last treatment to harvest and why the pest control material is needed. The form also inquires if any preliminary data are available. Preliminary data are very important because they are often needed to convince the agricultural chemical companies that the proposed use is safe when used on the crop and it effectively controls the target pests.

Upon receipt of the completed PCR, the proposed use is screened by IR-4 personnel for validity. The basic query includes questions such as Is the proposed use already registered? Will the agricultural chemical company which holds the US registrations for the chemical be willing to cooperate with IR-4 to obtain the regulatory

Biological activity

Active as blossom thinner in apple (*Malus domestica*).
Plant growth regulator that improves harvest management by inhibiting ethylene biosynthesis in numerous tree fruit.
Assists in retention and size of cotton (*Gossypium* sp.) bolls.
Hybridizing agent on barley (*Hordeum vulgare* ssp. *vulgare*) wheat (*Triticum* sp.) and soybean (*Glycine max*).
Desiccant and harvest aid on potato (*Solanum tuberosum*).
Protects the apple and pear (*Pyrus communis*) fruit from scald.
Controls sprout on storage potatoes.
Enhances crop growth and yield in numerous vegetable crops.
Manages the crop load on apple.

Novel PGR that promotes sugar accumulation in processing oranges (*Citrus sinensis*).
Inhibits the attachment of ethylene to ethylene receptor for a postharvest storage extension in numerous fruits and vegetables.
Shortens plant internodes and plant height on cotton and grapes (*Vitus* sp.).
Ripening and shelf life enhancement on numerous fruit and vegetables.
Reduces vegetative growth-better balance between canopy development and fruit production in numerous fruits and vegetables.
Increased nutrient uptake, resulting in improved yields on most crops.
Growth regulator with use resulting in less potential for lodging, more efficient ryegrass (*Secale cereale* ssp. *cereale*) seed set and harvest.

clearance of the pest control tool? and Are there any regulatory impediments known that may delay or result in denial of the registration? To answer some of these questions, IR-4 formally submits a questionnaire to the appropriate agricultural chemical company to determine if they are willing to expand the registration to include the IR-4 suggested use once IR-4 develops the appropriate data. For food crops, IR-4 develops data that determines the amount of chemical remaining on the crop at harvest. This is called a Magnitude of the Residue study. For nonfood crops, IR-4 develops crop safety and/or product performance data. If so, the proposed use is regarded as researchable and is considered in the research project prioritization procedures.

Unfortunately, IR-4 does not have sufficient resources to conduct research on all proposed researchable projects. In fact, for every research project IR-4 funds, there are approximately five projects delayed pending additional resources. Because of this shortfall, IR-4 strives to work on the most important projects.

The Food Use and Ornamentals Workshops are the cornerstone of the IR-4 priorization process. These are open forums where over 200 minor crop growers, commodity organization representatives, agricultural chemical company representatives, and federal and state research/extension scientists attend and participate. At the workshops, every potential project is discussed in detail and its importance is considered on such factors as the availability and efficacy of alternatives, pest damage potential, performance of the proposed chemical, and its integrated pest management program (IPM) compatibility. From the workshop participants, three tiers of priorities projects are identified. Priority A, the highest tier, are the most important projects. Because of their importance, IR-4 will begin research work at the next practical experimental start date. All efforts will be made to submit results of Priority A research to EPA within 30 months of protocol approval. The next tier projects, Priority B, are also important, but funding may not be available. IR-4 will use its resources in the most efficient manner to complete as many of these projects as soon as possible, given funding restraints. The final tier projects, Priority C, are considered of less importance than Priority A and Priority B projects. IR-4 will conduct research on these projects only after all Priority A and Priority B projects are conducted, which usually is unlikely.

Though IR-4 follows the priorities set at the workshops very closely, there are occasions when the EPA or the cooperating agricultural chemical company will recommend that IR-4 delay initiation of research for a specific chemical. IR-4 usually heeds this advice and delays or cancels research pending satisfactory handling of the outstanding issue(s).

The IR-4 Project's participation in the regulatory clearance with plant growth regulators on food crops is limited. In fact, only 128 requests for assistance have been submitted for plant growth regulators. In contrast, over 8000 requests for assistance have been submitted for crop protection chemicals. It is not clearly understood why there have not been more requests for IR-4 assistance with plant growth regulators in food crops. It is very clear that there are growth regulator needs in horticulture crops. It could be due to multiple factors including the limited spectrum of plant growth regulators, the lack of researchers in USDA and the agricultural experiment stations in this area, and the low interest by industry to support the registration due to real or perceived crop damage liability. Of the 128 requests for assistance, IR-4 has participated in the regulatory clearance of 19 plant growth regulator uses. This includes the registration of 2,4-D on grapefruit (*Citrus×paradisi*) to stop fruit drop, sucker suppression in hops (*Humulus lupulus*) with endothall, a harvest aid in macadamia nuts (*Macadamia integrifolia*) and guava (*Psidium guajava*) with ethephon, gibberellic acid on numerous crops for multiple uses, and NAA on citrus (*Citrus* sp.) and pome fruit (Rosaceae).

In addition to the above, IR-4 has current active research/regulatory programs with several plant growth regulators on minor food crops (Table 1). The IR-4 Project has been more active in plant growth regulators in nonfood crops. Since 1977, IR-4 has received 311 requests to provide assistance in obtaining national registrations for 14 plant growth regulators in nursery, floral, forestry and turf production and maintenance. These include the following: 6-benzylamenene, ancymidol, chloroflurenol, chlormequat chloride, chloromequat chloride + daminozide, chloropropham, daminozide, ethephon, flurprimidol, gibberellic acid, methyl esters of fatty acids, NAA, paclobutnazol, prohexadione calcium and uniconazole. Sixty-six national registrations have been obtained as the result of IR-4 sponsored research with these chemicals on ornamental crops. In addition, two special local needs (state only) registrations have been supported by IR-4 data. Research plans for 2001 include new plant growth regulators on several ornamental crops.

As noted previously, it has been recognized that the IR-4 Project is involved with the leading edge of new pest control technology. IR-4 recognized the tremendous innovative discovery process being undertaken in the mid-1990s by the crop protection companies to develop new, reduced risk chemistries and more effective biopesticides to solve pest control problems with minimal impacts on human health and the environment. The IR-4 Project estimates there were more new chemicals and biopesticides discovered in the decade of the 1990s than the previous four decades combined. IR-4 has developed a proactive strategy to encourage the crop protection industry to consider working with IR-4 to develop minor crop strategies at the same time they make their commercialization decisions on major crops like corn, cotton, soybeans and small grains. The key point of the strategy is to show industry that minor crops can collectively become significant source of revenue and working in cooperation with IR-4 to achieve minor crop registrations can be beneficial. It is the goal of the IR-4 Project to have these new minor crop tools available at the same time or shortly after the major crop registrations.

There are several new plant growth regulators that are encouraging. Many of these are outlined in Table 2. These include aminoethoxyvinylglycine or AVG which is marketed as Retain by Valent BioSciences (Libertyville, Ill.). This material is a glycine analog which improves harvest management by inhibiting ethylene biosynthesis. AVG is already registered on pome fruit, and has potential on stone fruit) (*Prunus* sp.) cucurbits (Cucurbitaceae), tomato (*Lycopersicon esculentum*) and cotton. *Bacillus cereus* is a new plant growth

regulator from Microflo (Memphis, Tenn.). It is a biological that is registered on cotton that assists in boll retention and increasing boll size. MBTA-HCl is marketed by Valent Bioscience as Ecolyst. The active ingredient in this product, diethyl-2-(4-methylbenzyloxy) ethylamine hydrochloride is a novel plant growth regulator that promotes sugar accumulation in processing oranges (*Citrus sinensis*). It is already registered on orange and progress is being made through IR-4 to extend the registration to grapefruit. BASF (Research Triangle Park, N.C.) and Kumiai Chemical Industry Co. (Tokyo) have a new plant growth regulator that they are selling in the US. Its trade name is Apogee and contains the active ingredient prohexadione calcium. This chemical reduces vegetative growth, allowing a better balance between canopy development and fruit production. Apogee is already registered on apple (*Malus domestica*), pear (*Pyrus communis*), pea (*Pisum sativum*), and *peanut (Arachis hypogaea*). It has potential on rice (*Oryza sativum*), sweet cherry (*Prunus avium*), hop, mint (*Mentha* sp.), seed potato (*Solanum tuberosum*), strawberry (*Fragaria ×ananassa*), sweet potato (*Ipomoea batatas*), avocado (*Persea americana*) and mango (*Mangifera indica*).

For more information on other new plant growth regulators and other new crop protection chemistries and biopesticides visit the IR-4 web site at <www.cook.rutgers.edu/~ir4> (Baron, 2001). This site also contains general information about the IR-4 Project, access to current news briefs and quarterly newsletters, access to the Project's data base to allow tracking of progress with research projects and requests for assistance and information about Ornamental and Biopesticide research objectives. And as mentioned before, you can also use the web site to complete and submit a Pesticide Clearance Request for IR-4's assistance.

Literature cited

Baron, J.J. 2001. Interregional Research Project #4 Project; The Minor Use Project. 25 October 2001. http://www.cook.rutgers.edu/~ir4