

## THE REGULATION OF BUGOIL: EXPERIENCES FROM NORTH AMERICA AND THE EU

David Marks, Plant Impact, Preston, UK compares the registration approaches applied by the US and EU regulatory agencies

### Key words:

*Thymus vulgaris*, *Tagetes erecta*, *Gaultheria procumbens*, Biopesticide.??

### Introduction

Current popular opinion increasingly favours a reduction in the use of pesticides, lower residues and a move towards sustainable agricultural practice.

Achieving this goal needs change in two areas. Firstly, regulation needs to change to tighten up registration and use of existing agrochemicals. This is already well underway in the major markets.

Secondly, new products are needed – products with excellent efficacy, and a safe environmental profile. Safer products need not be natural (indeed many natural products are less safe than the best conventional agrochemicals!). Nevertheless safe natural products with efficacy to match the best conventional agrochemicals and a safe environmental profile are the kind that governments, consumers, NGOs and the food industry are keen to see being developed and introduced.

However, natural products are often chemically very different to the synthetic single active ingredient pesticides that they can replace. Therefore, the existing registration systems that are designed to ensure safe use of conventional pesticides are often fundamentally unsuitable to natural product registrations.

This can lead to a conflict. Governments rightly want to make existing conventional pesticides safer, and, in order to achieve this, need to increase their regulation of them in order to improve standards. Whilst this trend has undoubtedly led to a dramatic and welcome improvement in the environmental impact of conventional pesticides, it has also led to the less desirable outcome whereby environmentally friendly natural pesticides have also become increasingly difficult to register, slowing down or even preventing market entry of safer, sustainable products.

This situation must be addressed, or industry will be reluctant to invest in research programmes for development of natural pesticides. This will slow progress towards sustainability.

This article concentrates on a plant-derived pesticide (BugOil) derived from Plant Impact's patented chemistry. It looks at two different approaches to registration of the product (the USA and EU regulatory systems), and compares

them. It then discusses how natural products are variable and that perhaps in future regulatory systems may need to be flexible in order to fast track the safe products, but be sufficiently robust on the less safe ones.

### What is BugOil chemistry?

Before discussing the regulatory systems let us first describe the product.

BugOil is based on a natural plant derived pesticide chemistry developed by Plant Impact plc. It harnesses a powerful synergy between 3 natural plant essential oils (*Tagetes erecta*, *Thymus vulgaris*, *Gaultheria procumbens*) encapsulated in a food grade vegetable oil/ emulsifier base. BugOil is a Plant Impact product based on patented chemistry.

The essential oils used in BugOil are all present at lower levels than in the plants from which they are extracted from. They are also all used in food in both the USA and the European Union at levels higher than in the product.

BugOil has been proven in GEP trials to control mites, whitefly and aphids to the same excellent level of efficacy as current best-performing industry benchmarks (including avermectin and imidacloprid). It gives quick knockdown and long lasting repellency (up to 48 days observed in some crops).

BugOil is extremely safe to non-target organisms (mammals, fish, birds) and most beneficial insects (including bees, earthworms, ladybirds and lacewings). It is biodegradable and leaves no unnatural residues or taint on crops.

Additionally, BugOil has a very good resistance profile – no resistance has been seen in studies testing against resistant

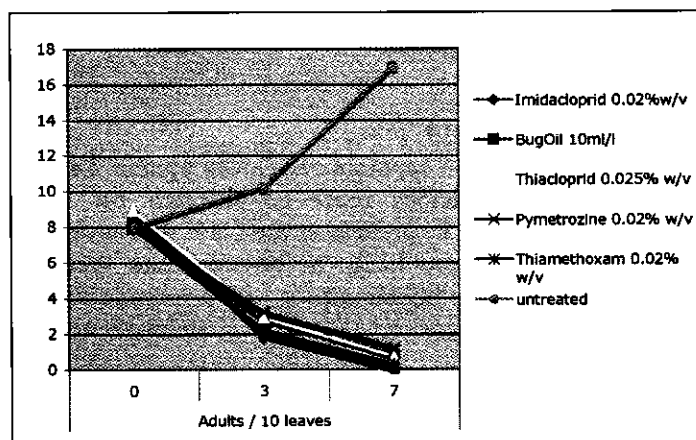


Figure 1. GEP trial (Holland 2005): Cotton aphid (*Aphis gossypii*), *Chrysanthemum* (adults/leaf).

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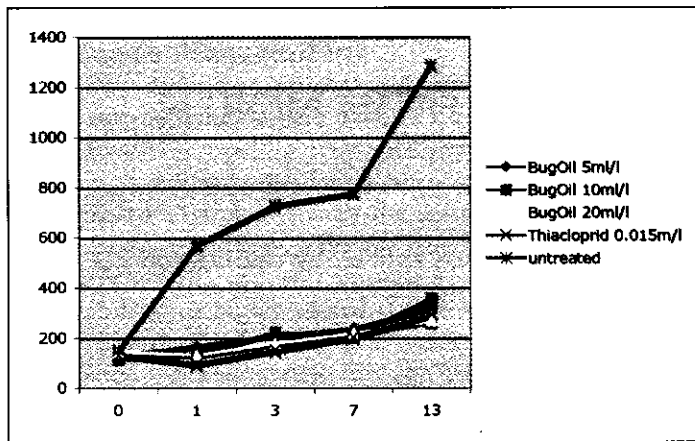


Figure 2. GEP trial (Spain 2004): Whitefly (*Bemisia tabaci*), Zucchini (adults/ 10 leaves), zucchini

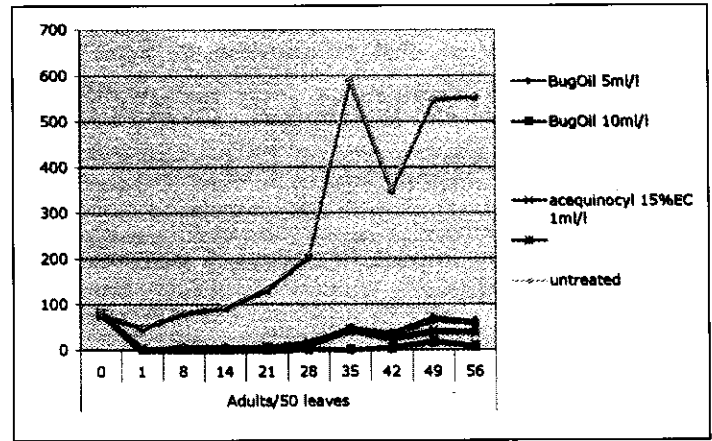


Figure 3. Trial (Japan 2004) Citrus red mite (*Panonychus citri*), Satsuma

insect populations with known resistance mechanisms (Rothamsted Research).

BugOil is exactly the sort of high efficacy, low environmental impact, sustainable technology that is sought after by the food industry, government and consumers. The regulation of products based on this chemistry is discussed in this article.

### USA regulatory system

The US regulatory system has several routes: conventional registration (for traditional synthetic ai chemistry-based agrochemicals); Bio-pesticide registration (for natural products); and lastly Minimum risk pesticides (EPA exempt).

The US system differentiates between products formulated from natural chemicals, biological organisms and synthetic ai chemistry-based agrochemicals. This allows the system to ensure that products are safe and effective, whilst recognising that bio-pesticides are fundamentally different in their make-up and need to be assessed in a different way.

By separating bio-pesticides from conventional pesticides it allows both types of chemicals to be rigorously evaluated in a way suited to the chemical nature of the product. The main difference in the systems is in testing and Quality Control (QC) requirements. Natural products are often so different to conventional agrochemicals that they need very different testing methods.

### EU regulatory system

In the EU, there is no separate regulatory system for bio-pesticides. All pesticides must go through the same registration process. The premise in the EU is that as natural chemicals are no more likely to be safe than synthetic chemicals they require the same registration procedure.

It is certainly true that not all natural compounds are safe (far from it). The first commercially produced pesticide (nicotine) was both natural and toxic to humans and other non-target organisms.

It is also true that not all natural pesticides have a good environment profile. In fact the most commonly used plant extract active ingredients pyrethrum, rotenone and

azadirachtin (Neem) are all broad spectrum and, therefore in some respects, worse for the environment than more selective conventional agrochemicals.

From this point of view it is reasonable not to give an 'easy ride' to natural products. However what then is to be done with products that are obviously safe? As BugOil could be sold as a food product in EU supermarkets (with no regulation), but when applied to food in dilute form it requires regulation.

To this end, the EU published guidelines to the national regulatory bodies giving guidance on how to deal with natural product registrations. These guidelines allow flexibility from the authority taking the product to Annex 1 registration. In areas such as toxicology, they can, at their discretion, accept logical argument and public domain evidence in lieu of data (data waiver arguments).

Taking the example of BugOil and environmental fate, a data waiver argument could be constructed that environmental fate in soil tests should not be required as the crops from which the essential oils are extracted have higher levels of essential oil than the undiluted product, and have been grown in the EU for many years with no reported problems.

The positives to this approach are that the regulators can ensure that products are consistent and efficacious (important to all products regardless of their safety), but can be relaxed on testing requirements where appropriate (and not where not appropriate).

The negative aspect of this system is the lack of clarity. The national regulatory bodies all interpret the guidelines differently, and there is a tendency with some many to be dogmatic and insist on applying standard rules to all products.

The issue here is that natural products are not standard. They work differently to conventional agrochemicals based on discrete active ingredients. To get the best out of natural chemicals they require a fresh approach, and many need to be used in combination, or in different types of formulation to conventional agrochemicals.

This means that in order to pass standard tests, products are forced to be more like the conventional chemicals for which the regulations were originally designed. This

situation can stifle innovation as it makes it difficult for less conventional chemistry (no matter how efficacious) to gain a registration. What this ultimately produces is natural products with discrete single active ingredients; just like existing synthetic agrochemicals. Natural products that are similar in design to conventional agrochemicals are likely to encounter many of the same problems. Take the example of spinosad and abamectin – which are now encountering resistance problems.

Until there is clarity in the system, the EU will continue (as is the case currently) to lag behind the USA in the commercialisation of bio-pesticides. This is deleterious to the EU pesticide industry, EU farmers, EU consumers and the EU environment.

## What is best practice for registration of natural products?

As more natural chemistry is developed the regulators will need to change. There are areas where regulations should not be relaxed for any product whether safe or unsafe and whether natural or synthetic.

**Efficacy** – No allowance should ever be made for lack of efficacy. Natural products that do not work effectively are no good to anyone, and harm the image of bio-pesticides. BugOil performs to the same standards as the best conventional chemicals, this should be the benchmark expected of any new pesticide.

**Quality control** – Natural products can be highly variable. It is not always possible to keep them as consistent as a conventional agrochemical, but they should always have a Q/C method that can ensure consistency of formulation. This is important to avoid issues of variable performance.

Plant Impact has developed GLP test procedures for marker chemicals in the components of products based on Plant Impacts chemistry. This ensures that the product can be tested to ensure that there is no batch-to-batch variation. This is an important requirement in the EU registration guidelines for plant derived pesticides.

There are also areas where *some* natural products should avoid regulation. If a compound is already in the environment and the food-chain is it reasonable for it to have the same

requirements as compounds like organophosphates with known high levels of toxicity? As many natural compounds are neither safe, nor any better for the environment than conventional agrochemicals there should certainly be no blanket relaxation on natural products.

One of the reasons bio-pesticides are put through a conventional registration process is that natural does not always equate to safe. Indeed many of the most toxic substances known to man are plant derived. Therefore, it is not sensible to have wide ranging exemptions purely due to the natural nature of products. Natural products should be required to be at least as environment friendly as the synthetic pesticides with which they are to compete.

## Benefits of change

So what are the benefits of changing regulations?

**Increased novelty** – If regulation continues to set the same obstacles for natural products as for synthetic products it will limit the types of new chemistry that are developed. Regulating in the same way, leads to natural products that are essentially very similar to conventional agrochemicals, and makes it difficult to introduce more novel chemistry. As natural products are much more variable in terms of source and chemistry they require a more flexible approach. Rigid and inflexible regulation leads to a lack of novelty.

**Increased R&D** – The US has a system that is considerably more flexible than the EU, over time this will increasingly give the US a competitive advantage. If it is easier for biotech companies to trade there, then the US will attract more investment into biotech ventures than in the EU (this is already the case). If the EU does not lighten the regulatory burden it will continue to lag behind in availability of bio-pesticides.

**Improved farming** – Ultimately allowing farmers access to a greater range of chemicals (especially safe and efficacious chemistry) improves profitability for the farming industry, and benefits consumers and the environment. In short, reducing the regulatory burden can benefit all stakeholders.

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