PYRITHIOBAC-SODIUM

in the product

DU PONT STAPLE HERBICIDE
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in the product

DU PONT STAPLE HERBICIDE

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National Registration Authority for
Agricultural and Veterinary Chemicals.
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1996
PUBLIC RELEASE SUMMARY DOCUMENT

EXECUTIVE SUMMARY

Introduction

The purpose of this document is to provide a summary of the data reviewed and an outline of regulatory considerations for the proposed registration of the chemical pyrithiobac-sodium in the product Du Pont Staple Herbicide as a post-emergence herbicide for control of certain broadleaf weeds in cotton. Use in NSW and Qld only is proposed.

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) invites public comment before deciding whether to proceed to approve this product for use in Australia.

The NRA has completed an assessment of the data submitted by the applicant in support of this use of pyrithiobac-sodium and has provided the following information for public comment:

Agricultural Aspects

Du Pont Staple Herbicide is a new herbicide containing 850 g/kg pyrithiobac-sodium. The product can be sprayed over the top of cotton and has been shown to give good control of broadleaf weeds in cotton at rates of between 30 and 120 g/ha. Registration of the product is sought in NSW and Qld only.

Environmental Aspects

DuPont Staple Herbicide will be formulated as a water soluble powder to be used alone, or in conjunction with other commercially available herbicides, to control broadleaf weeds to replace manual chipping of weeds and the use of shielded sprays. It will be used once a season, although it may be applied again if no crop damage was observed after spraying. Pyrithiobac sodium is a benzoate herbicide which inhibits acetolactate synthase. Staple Herbicide is to be registered for use on cotton only, which would therefore restrict its use to heavier clays and loams.

There is potential for Pyrithiobac sodium to be highly mobile, though its potential to accumulate in soils and plants appears limited. Degradation of Pyrithiobac sodium appears restricted to aqueous photolysis, and some metabolism in aerobic soils, both giving mineralisation to CO$_2$. Field dissipation studies, however, generally indicate rapid dissipation from the top layer (0-15 cm). The differences in half-lives between soil metabolism studies and field studies (about 60 days vs 12-46 days) would seem to indicate that factors other than metabolism or degradation could be responsible for the rapid dissipation observed in some field studies.

The ecotoxicity profile of Pyrithiobac sodium suggests that the area of concern is non-target terrestrial and aquatic plants. For non-target plants, it is expected to be phytotoxic
to various degrees. Animals in general, including aquatic and beneficial invertebrates, were noted to be much less sensitive to Pyrithiobac sodium.

Toxicology

Pyrithiobac-sodium has low acute oral, dermal and inhalation toxicity, is a slight eye irritant, and does not cause skin irritation or sensitisation. A formulation very similar to Du Pont Staple® Herbicide has low acute oral, dermal and inhalation toxicity, and does not cause skin sensitisation, although it is a moderate eye and slight skin irritant.

The main target organ for pyrithiobac-sodium is the liver. Prolonged high dose oral administration of pyrithiobac-sodium to mice, rats and dogs resulted in increased liver weights, which may be secondary to an increase in liver cell size. After 18 months to 2 years of chronic dosing in rats and mice, the increase in liver weight, which may be adaptive, progressed to liver cell damage. In addition to the liver cell damage, kidney damage was seen in mice and rats following 18 months to 2 years of high dose dietary exposure to pyrithiobac-sodium.

Anaemia was a feature in rats and dogs after high doses of pyrithiobac-sodium. In rats, anaemia appeared to be transitory, with red blood cell parameters returning to within normal limits by 12-18 months. A reduction in white blood cell numbers was noted in mice and rats, and may, like the anaemia, be related to a primary bone marrow depression caused by pyrithiobac-sodium.

An increase in the incidence of renal tumours was noted in rats. The negative in vitro mutagenicity test and in vivo mouse bone marrow micronucleus assays suggests that the tumours may not be caused by damage to genetic material.

Based on an assessment of the toxicology, it was considered that no adverse effects on human health would be expected when the product is used in accordance with label directions.

Residues

Residue data were presented for cotton, cotton seed and the processed cotton seed oils, from trials conducted in Australia and overseas.

In lint, cotton seed, delinted seed, crude oil, meal, refined oil, cotton seed hulls and soap stock, residues were not detected.

Occupational Health and Safety

Worksafe Australia has conducted a risk assessment on DuPont Staple Herbicide and concludes that it can be safely used by workers.

Pyrithiobac-sodium is not a hazardous substance. The formulated product, DuPont Staple Herbicide, however, is considered to be a hazardous substance. The product is of low acute toxicity but may cause skin and eye irritation.
DuPont Staple Herbicide will be imported fully formulated in water soluble bags and re-packaged into sales packs in Australia.

Because DuPont Staple Herbicide is enclosed in water soluble packaging, end users are not required to directly handle the concentrated product so exposure will be much reduced at mixing.

The product may be applied by ground or aerial spraying. Spraying this product is not expected to result in health effects in end users.

Safety directions warn users to avoid contact with eyes and skin, however specific personal protective clothing is not considered necessary for workers preparing and using the spray. All workers should adopt good occupational hygiene practices.

No re-entry period is necessary for workers re-entering treated areas.

DuPont Staple Herbicide can be used safely if handled in accordance with the control measures indicated on the label. Additional information is provided on the material safety data sheet for the product.

**Trade**

Du Pont Staple Herbicide is not expected to have an impact on Australia’s trade with other nations. Residues of pyrithiobac-sodium could not been detected in produce from cotton crops treated with the product.
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INTRODUCTION

The purpose of this document is to provide the public with a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical pyrithiobac-sodium as a post-emergence herbicide for control of certain broadleaf weeds in cotton, and to seek public comment prior to the chemical product being approved for use in Australia. Responses to the public consultation will be considered prior to registration of the product and will be taken into account by the NRA in deciding whether a product should be registered and in determining appropriate conditions of registration and product labelling. Copies of full technical reports are available on request from the NRA.

Comments should be received by 14 July 1996 and sent to:

Ms E Taverner
Agricultural Registration
NRA
PO Box 240
Queen Victoria Terrace ACT 2600
FAX: (06) 272 3218

Applicant

Du Pont (Australia) Limited has applied for registration of a post-emergence herbicide product containing a new active constituent, pyrithiobac-sodium, a benzoate herbicide which inhibits acetolactate synthase.

Product Details

Pyrithiobac-sodium will be marketed under the trade name Du Pont Staple Herbicide as a water soluble powder formulation containing 850 g/kg of active constituent.

Du Pont Express Herbicide will be imported fully formulated in water soluble plastic bags, requiring packaging into outer cartons only in Australia.

Du Pont (Australia) Limited intends to market Du Pont Staple Herbicide in NSW and Qld only for the post emergence control of broadleaf weeds in irrigated and dryland cotton.
CHEMICAL PROPERTIES

Active Constituent

The chemical active constituent pyrithiobac-sodium is manufactured in the US and has the following properties:

Common name (ISO): pyrithiobac-sodium
Chemical name: sodium 2-chloro-6-(4,6-dimethoxypyrimidin-2-ylthio) benzoate
Product name: DuPont Staple Herbicide
CAS Registry Number: 123343-16-8
Empirical formula: C$_{13}$H$_{10}$ClN$_{2}$NaO$_{4}$S
Molecular Weight: 348.1
Physical form: powder at ambient temperature
Colour: pale yellow
Odour: faint, ester like
Melting point: 233.8 to 234.2°C
Density: 1.609
Octanol/water partition coefficient ($K_{OW}$): 2.12 at pH 3, 0.60 at pH 5, -0.84 at pH 7, -1.23 at pH 9
Vapour pressure: <4.8 x 10$^{-9}$ Pa

Structural Formula:

![Structural Formula]

Formulated product

The active ingredient pyrithiobac-sodium is formulated into the agricultural chemical product DuPont Staple Herbicide at either of two manufacturing sites, one in the US and the other in Japan. DuPont Staple Herbicide is a water soluble powder formulation of pyrithiobac-sodium. The fully formulated product is imported into Australia packed in water soluble bags.
AGRICULTURAL ASSESSMENT

Justification for Use

Pyrithiobac-sodium is a new compound which provides selective control of a number of broadleaf weeds of cotton crops, namely: annual ground cherry, anoda weed, Bathurst burr, bellvine, Boggabri weed, cowvine, Noogoora burr, Polymeria, Sesbania pea, thornapple, volunteer sunflower, wild melon and yellow vine. DuPont Staple Herbicide exhibits low toxicity to cotton plants. It can therefore be applied by spraying over the top of cotton with minimal damage to the cotton crop itself.

DuPont Staple Herbicide has the potential to provide the cotton industry with a new method for controlling hard to kill weeds which have previously been removed by manual workers with hoes (known as cotton chippers) or with shielded sprays, which have a high potential for crop damage.

The reviewers consider that this herbicide has the potential to have a big impact on the broadleaf herbicide market, with a possible reduction in the use of herbicides by the cotton industry.

Proposed Use Pattern

DuPont Staple Herbicide can be used on both irrigated and dryland cotton by ground application. The label recommends that post-emergence applications of DuPont Staple Herbicide can be made from the first true leaf stage to early flowering of the cotton plant. The correct leaf stage for application to the individual weeds is specified on the label. In some cases, suppression rather than full control is claimed at later weed growth stages.

Application rates vary according to the weed species, with rates varying from 30 to 120 g/ha.

The product may be applied as a band or directed spray, or as a blanket spray over the top of the crop.

It can also be used to control Sesbania Pea by air under certain conditions. Sesbania Pea grows very rapidly and infestations can get out of control if conditions are against ground application. In this situation the only way to salvage the crop is to apply the herbicide by air.

The label warns against aerial spraying in still conditions and in winds likely to cause drift onto adjacent sensitive crops or fallow areas likely to be planted to these crops. The spray boom must be turned off whilst passing over creeks, dams, channels and rivers. There is a warning against aerial application when a temperature inversion is likely to occur.
Evaluation of Efficacy

Efficacy data provided in support of registration of the product was reviewed by experts in New South Wales Agriculture and Queensland Department of Primary Industries. The reviewers considered that the data supported the claims made on the label of the product and recommended registration of the product.

Phytotoxicity

The label warns that there may be some initial leaf yellowing or biomass reduction of the cotton plants after spraying with Staple. This is a temporary effect. The product can be used more that once in a season if there has been no crop damage.

The product is not recommended for use on cotton growing under stress caused by weather, insects or disease, nor for weeds that are stressed or not actively growing.

Resistance management

DuPont Staple Herbicide is a member of the benzoate group of herbicides. The mode of action is acetolactate synthase (ALS) inhibition. For weed resistance management the product is a group B herbicide. The label warns against the prolonged use of ALS inhibitor herbicides on the same weed population and recommends that ALS inhibitors should not be used if the user suspects that resistant weeds are present.

Conclusion

The NRA considers that DuPont Staple Herbicide will control the weeds claimed on the label when used according to the label directions.
ENVIRONMENTAL ASSESSMENT

Environmental fate

Pyrithiobac sodium at 850 g/kg is the active ingredient in DuPont Staple Herbicide formulated as a water soluble powder. It is to be used alone, or in conjunction with other commercially available herbicides to control broadleaf weeds to replace manual chipping of weeds and the use of shielded sprays. It will be used once a season, although it may be applied again if no crop damage was observed after spraying. Pyrithiobac sodium is a benzoate herbicide which inhibits acetolactate synthase (ALS). Staple Herbicide is to be registered for use on cotton only, which would therefore restrict its use to heavier clays and loams.

- Degradation

Pyrithiobac sodium is hydrolytically stable in buffered solutions with a pH range of 5-9. In aqueous photolysis studies, however, its half-life (assuming 12:12 photo:scotophase) ranged from 8.7 to 15.3 days with a slight influence of pH on degradation (increased rate of degradation with increasing pH).

The results of a soil photolysis study suggest some initial photodegradation might occur, but will not be a significant degradation mechanism in soil. At the end of the study (15 d), 82% of the labelled phenyl ring, and 69% of the labelled pyrimidine ring was recovered as parent compound in treatment groups. Assuming a 12:12 photo:scotophase, the half-lives Pyrithiobac sodium and were 110 d and 62 d (phenyl and pyrimidine label, respectively). The predominant product of degradation of the radiolabelled phenyl ring was $^{14}$CO$_2$ (11.5% of applied radioactivity), while that of the pyrimidine ring was urea (11%).

- Metabolism

In an aerobic soil metabolism study, the half-life of $^{14}$C-Pyrithiobac sodium was about 60 days. Volatile $^{14}$C (CO$_2$) from degradation in the non-sterile soil at the end of the study (1 year) was >60% of the applied radioactivity. The amount of label which could be extracted from non-sterile soil at the end of the study period was about 10%. No single metabolite was >10%. In sterile soil, no degradation occurred. Residues (>10%) were associated with the humin, humic acid, and fulvic acid soil fractions. The primary degradation of Pyrithiobac sodium was through complete mineralisation to CO$_2$.

No firm conclusions on an anaerobic soil metabolism study on Pyrithiobac sodium could be made due to different observed trends for each label; the company attributed this to experimental error, but concluded that metabolism at least slowed. A conservative approach would be to conclude no metabolism occurred under anaerobic conditions. Under irrigated field conditions, soils might become anaerobic when the cotton crop is flooded (100 mm of water standing in the irrigation furrows) and cracks sealed.
• Mobility

In soil flask adsorption/desorption studies with Pyrithiobac sodium and 4 soils, both processes were described by Freundlich isotherms. The adsorption and desorption coefficients based on organic carbon content of soils ($K_{a,om}$ and $K_{d,om}$, respectively) were calculated to be from 4.9 to 34, suggesting that it is likely to be weakly bound and highly mobile in soils.

Mobility of Pyrithiobac sodium was further assessed with soil thin layer chromatography on 4 soils. The $R_f$ values indicated that Pyrithiobac sodium will have similar mobility to bromacil, and possibly saccharin (ie classed as mobile to very mobile), while its metabolite, O-desmethyl-Pyrithiobac sodium, will have similar mobility to saccharin (ie classed as very mobile). Similarly, column soil leaching studies indicated that Pyrithiobac sodium is likely to be mobile, even after ageing, with the majority of the substance in the leachate; one soil (silty clay, not aged) however, had only 20% of the applied radioactivity in the leachate.

• Field dissipation

In a study in two field sites in the US representing a situation typical for dryland cotton, residues were only detected in the top 0-15 cm of soil for each soil. Further, there was rapid dissipation of Pyrithiobac sodium from this layer, with a calculated $DT_{50}$ of 14.1 days and 10.8 days, and $DT_{90}$ of 86.3 days and 48.8 days, for a silt clay loam and clay loam soil, respectively. In another study on a sandy loam representing a situation typical for irrigated cotton for irrigated cotton in the USA, results reflected more closely the laboratory studies, with a half-life of 46 d. In this study, Pyrithiobac sodium was found throughout the soil layers 180 days after application. Results also clearly demonstrated that loss of parent was due to metabolism. The occurrence of parent compound at depths below the surface layer was coincidental with a decrease in potential evaporation rate while the level of combined irrigation and rainfall was maintained.

• Groundwater Study

The company has supplied details of a groundwater study being performed as part of the provisional registration of this product in the United States. There are two phases of the study, with phase 1 the identification of the worst case most vulnerable site for movement of Pyrithiobac to ground water, and phase 2 the reporting of the results of the study (due to be completed in 1997). The company has agreed to provide the results of the study when they become available.

• Accumulation studies

Radioactivity in a confined plant accumulation/metabolism study reached about a third of the initial level 120 days after application and then remained relatively stable. Most of this radioactivity was retained in the top half of the soil (to a depth of 12.5 cm), even 300 days after application, and was recovered from soil mostly as bound degradation products (50-80% of total radioactive residues), associated with the fulvic
and humic acid, and humin fractions. By the end of the study (392 days after application), the level of parent compound had decreased to 5% of the applied radioactivity.

• Conclusion

Given the above, there is potential for Pyrithiobac sodium to be highly mobile, though its potential to accumulate in soils and plants appears limited. Degradation of Pyrithiobac sodium appears restricted to aqueous photolysis, and metabolism in aerobic soils, both giving mineralisation to CO₂ (it appears to be moderately persistent in laboratory studies). Field dissipation studies, however, indicate rapid dissipation from the top layer (0-15 cm), but with some potential for leaching.

Environmental effects

Results using the TGAC for the following are available birds, fish, aquatic plants, and bees. Some data can be gained for effects on mammals and non-target terrestrial plants from toxicological and plant accumulation studies. The following gives summaries of the studies in this area:

Avian toxicity studies

Five-day oral (acute) tests with Bobwhite quails gave an LC₅₀ of 1599 mg/kg, while five-day dietary (acute) tests with Bobwhites and Mallards gave an LC₅₀ > 5620 mg/kg. One-generation studies with each of the above species showed no treatment-related mortality, overt signs of toxicity (including for eggs or offspring), or treatment-related effects on body weight were observed in the mallard study or Bobwhite study, resulting in a NOEC of 1500 ppm (highest test concentration) in each study. This data suggests that Pyrithiobac sodium is practically nontoxic to birds.

Aquatic Toxicity

The aquatic toxicity of Pyrithiobac sodium to bluegill sunfish, channel catfish, rainbow trout, sheepshead minnow, fathead minnow, water flea, crayfish, mysid shrimp, mcllusc, green algae, blue-green algae, freshwater diatom, marine diatom and duckweed. The results are given in Table 1.

The most sensitive aquatic species was the duckweed with an EC₅₀ (14 days) as 0.91 μg/L, and NOEC and LOEC of 0.50 and 1.0μg/L, respectively. The results indicate that Pyrithiobac sodium is practically non-toxic to fish and aquatic invertebrates, but varies from being very highly toxic to slightly toxic to aquatic plants, with EC₅₀'s ranging from 0.91 μg/L to 12 mg/L.
Table 1. Details and results of aquatic toxicity tests

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<td>Bluegill sunfish</td>
<td>96 h static</td>
<td>LC\textsubscript{50} &gt;930 mg.L\textsuperscript{-1}; NOEC = 930 mg.L\textsuperscript{-1}</td>
</tr>
<tr>
<td>Catfish</td>
<td>96 h static</td>
<td>LC\textsubscript{50} &gt;970 mg.L\textsuperscript{-1}; NOEC = 580 mg.L\textsuperscript{-1}</td>
</tr>
<tr>
<td>Rainbow trout</td>
<td>96 h static</td>
<td>LC\textsubscript{50} &gt;1000 mg.L\textsuperscript{-1}; NOEC = 1000 mg.L\textsuperscript{-1}</td>
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<tr>
<td>Sheepshead minnow</td>
<td>96 h flow-through</td>
<td>LC\textsubscript{50} &gt;145 mg.L\textsuperscript{-1}; NOEC = 145 mg.L\textsuperscript{-1}</td>
</tr>
<tr>
<td>Fathead minnow</td>
<td>42 d flow-through</td>
<td>NOEC = 100 mg.L\textsuperscript{-1}</td>
</tr>
<tr>
<td>Water flea</td>
<td>48 h static</td>
<td>EC\textsubscript{50} = 1100 mg.L\textsuperscript{-1}; NOEC = 1100 mg.L\textsuperscript{-1}</td>
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<tr>
<td>Crayfish</td>
<td>96 h flow-through</td>
<td>LC\textsubscript{50} = 910 mg.L\textsuperscript{-1}; NOEC = 910 mg.L\textsuperscript{-1}</td>
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<tr>
<td>Mysis</td>
<td>96 h flow-through</td>
<td>LC\textsubscript{50} = 140 mg.L\textsuperscript{-1}; NOEC = 140 mg.L\textsuperscript{-1}</td>
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<tr>
<td>Mollusc (shell deposition)</td>
<td>96 h flow-through</td>
<td>LC\textsubscript{50} = 130 mg.L\textsuperscript{-1}; NOEC = 130 mg.L\textsuperscript{-1}</td>
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<tr>
<td>Water flea</td>
<td>21 d chronic static-renewal</td>
<td>EC\textsubscript{50} = 289 mg.L\textsuperscript{-1} &amp; 360 mg.L\textsuperscript{-1}; NOEC = 260 mg.L\textsuperscript{-1}</td>
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<tr>
<td>Green algae</td>
<td>static 120 h</td>
<td>EC\textsubscript{50} = 107 μg.L\textsuperscript{-1}; NOEC = 23 μg.L\textsuperscript{-1}</td>
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<tr>
<td>Blue-green algae</td>
<td>static 120 h</td>
<td>EC\textsubscript{50} = 1.4 mg.L\textsuperscript{-1}; NOEC = 290 μg.L\textsuperscript{-1}</td>
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<td>Freshwater diatom</td>
<td>static 120 h</td>
<td>EC\textsubscript{50} = 12 mg.L\textsuperscript{-1}; NOEC = 6.7 mg.L\textsuperscript{-1}</td>
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<tr>
<td>Marine diatom</td>
<td>static 120 h</td>
<td>EC\textsubscript{50} = 9.6 mg.L\textsuperscript{-1}; NOEC = 7.8 mg.L\textsuperscript{-1}</td>
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<td>Freshwater macrophyte</td>
<td>static 14 d</td>
<td>EC\textsubscript{50} = 0.91 μg.L\textsuperscript{-1}; NOEC = 0.50 μg.L\textsuperscript{-1} (nominal concentrations)</td>
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Non-target Terrestrial Invertebrates and mammals

The LD\textsubscript{50} and LD\textsubscript{90} were determined for honey bee. The highest dose tested was 25 μg per bee with no apparent treatment-related mortality in any of the test concentrations. Therefore, it was concluded that Pyrithiobac sodium was relatively non-toxic to bees since the LD\textsubscript{50} was 11 μg per bee. Results of acute toxicity studies indicate Pyrithiobac sodium to be slightly non-toxic when ingested, slightly to moderately toxic by skin contact, and slightly toxic by inhalation.

Phytotoxicity

The herbicide is expected to have typical herbicidal activity (broad-leaved and non-specific) with inhibition of acetolactate synthase (ALS).

The “summary re-crop data” indicate it was safe to re-crop with barley and wheat 5 months after an application of STAPLE Herbicide at 120 and 240 g/ha, respectively. For sunflowers and soybeans, it is safe to re-crop 11 months after an application of Staple Herbicide at 240 g/ha. For both the summer and winter crops, cultivation prior to planting increases the crop safety.

In the section on Plant Accumulation above, phytotoxic effects were observed in all treatments and crops, resulting in differences in germination rates compared to the controls, and other effects after germination. These effects were even noted after 240 days of ageing in which only a few carrots survived at the lowest test level (140g/ha).

Prediction of environmental hazard

Hazard arising from use

Pyrithiobac sodium is proposed to be used to control certain broadleaf weeds in cotton. The main environmental hazard of Pyrithiobac sodium is from exposure to non-target plants. Environmental exposure of Pyrithiobac sodium may occur through:
- Lateral transport of the chemical in subsurface/groundwater flow;
- Contaminated rising water tables and/or irrigation water associated with accumulation of Pyrithiobac sodium in confined aquifers
- Spray drift to non-target areas; and
- Surface and tailwater run-off to non-target areas.

The latter two points have the greater potential for effect, although the first two points should not be ignored if Pyrithiobac sodium is moderately persistent in Australian soils as indicated in the field dissipation study\(^1\). In applying Staple Herbicide to cotton channels, surface run-off to non-target areas should be reduced if it is applied only when sufficient weeds are present to justify application, with most of the herbicide absorbed by the weeds, and when the soil is moist.

Worst Case Scenarios

- Aquatic hazard to aquatic flora and fauna from direct overspray onto water and from spray drift onto pond

The company provided an estimate of hazard based on the ecotoxicity results obtained for the fathead minnow, and concluded that “Staple Herbicide does not pose a risk to the aquatic environment by direct application or runoff”. The EFA agrees that Pyrithiobac sodium poses no significant hazard to aquatic fauna, but it could pose a significant hazard to aquatic flora. The EPA has calculated this hazard as follows: The Estimated Environmental Concentration (EEC) and Q for the worst case situation of direct overspray onto shallow water is 68, which reflects the very high toxicity to the aquatic macrophyte, *Lemna*.

For spray drift onto a shallow pond, the EPA assumes 10% of the applied formulation will drift, giving a Q of 6.8μg/L, and therefore still of concern. Its obvious very high toxicity to duckweed and green algae must be considered in its application and potential fate since it will be used in irrigated cotton. With appropriate labelling (see below), and following of label directions by operators of spray equipment (particularly in blanket and aerial spraying), this situation should not arise.

- Terrestrial hazard to invertebrates from direct spray onto soil

No data was provided for terrestrial fauna except for bees which showed that Pyrithiobac was relatively non-toxic. As the greatest impact of the herbicide is likely to arise from run-off into streams or application to areas where non-target plants occur, this is acceptable.

- Terrestrial hazard to birds from direct spray onto vegetation.

\(^1\)Australian soils are generally lower in organic matter and micronutrients, and have higher salt levels. In cotton growing areas, specifically, they are likely to have a heavier texture (ie greater clay content giving cracking clays) than those used in the field dissipation studies, although nutrient levels may be similar.
The company has provided an estimate of the hazard of Staple Herbicide to birds. Based on their calculations, there does not appear to be significant hazard (residues estimated at 1.2 mg/kg from plant metabolism studies, lowest LD50 of 1599 mg/kg for northern Bobwhite).

Potential for movement of Pyrithiobac sodium in the environment

The major factor that will influence Pyrithiobac sodium environmental exposure after its application will be its stability together with its potential to be highly mobile. With respect to these parameters, there has been no provision of data clearly relevant to Australian conditions. In a field situation other factors would also become important, such as net transpiration, stage of crop, degree of weed cover, actual rainfall, soil characteristics and timing of irrigation and other cropping practices.

In an ideal typical agronomic programme supplied by the company, there would be a 4-6 week period between the first Staple application and the first irrigation event. However, in actual use there would be no guarantee that this would occur, and the period would probably extend up to January, and include a second application for Noogoora burr. Water moving along the surface (eg from a rainfall event or poorly timed irrigation event) has the potential to shift Pyrithiobac sodium, not only along the channel but also into deep cracks.

The herbicide would also be metabolised by weeds, and band and directed sprays are likely to restrict the amount of herbicide reaching the soil compartment (particularly bottom of furrows), compared with aerial blanket spraying. Although the latter is likely to be only applied when weed densities are excessive, it would nevertheless result in greater environmental exposure. Although there is potential for residues to persist, applied chemical would also be intercepted by the crop and metabolised, as well as by the target weed.

The main contamination hazard is thus likely to result from runoff with most tailwater the result of rainfall because of restrictions on water use and current initiatives by the cotton industry and government to retain run-off on-farm. While the amended label now has a warning not to allow irrigation tailwater enter waterways or be used on other crops, and warns against application if rain may follow within 4 hours, this is likely to be insufficient to totally prevent off-farm movement of the herbicide. No conclusion can be made for the potential for Pyrithiobac sodium, on entering the soil compartment, to move through heavy, cracking clays, and its subsequent fate given its high solubility and unknown potential persistence and potential to leach. It is likely though that the American groundwater study is the worst case, and would give a sufficient indication of its mobility to groundwater, even in Australia, but will not provide sufficient information to evaluate the potential for Pyrithiobac sodium to contaminate surface waters.

Proposed use

Precautions should be taken to avoid contact with waterways/ponds due to Pyrithiobac sodium’s potential adverse effects on aquatic flora. When used as proposed on cotton the main hazard to the environment is likely to result from runoff, given its very high
toxicity to non-target plants (including aquatic plants). The draft label warns against application if rain or irrigation may follow within 4 hours.

Contamination from drift is expected to be negligible if applied according to label directions by experienced workers. The EPA also notes that its proposed use is to decrease the level of exposure of cotton workers (chippers) to pesticide residues. However, because:

- the data provided (e.g., lack of relevant metabolism and field dissipation data) do not give a clear indication of how the chemical will behave under Australian conditions, particularly its potential to contaminate surface waters,
- pesticide and herbicide use are of great concern to the cotton industry which is investing $5m to investigate the behaviour of existing chemicals, and
- it could be potentially very damaging to the cotton industry to introduce a major new chemical when the above aspects are not fully understood (i.e., potential for mobility and persistence of Pyrithiobac),

The EPA recommends that conditional clearance for the 1996/97 and 1997/98 growing seasons only be granted. Continued registration would be conditional on:

- The results of the American groundwater study being made available to the EPA when completed;
- A detailed strategy of how the company will conduct an aggressive stewardship campaign promoting STAPLE Herbicide in the lead-up to, and through, the 1996/97 growing season;
- Field trials are performed that address the potential run-off of Pyrithiobac sodium in heavy clays under Australian growing conditions;
- Fate (metabolism and half-life) of Pyrithiobac sodium in these soils, especially the potential for how movement into deep cracks might affect its fate; and
- The label amended by the addition of the following label restraint under “protection of wildlife, fish, crustacea and environment”:

  *Withhold irrigation as long as possible after application according to company advice on timing of application and irrigation.*

The results of the American groundwater study and Australian field studies will need to be reviewed before full product registration clearance is given.

The company has agreed in principle to the above conditions of registration.
PUBLIC HEALTH & SAFETY ASSESSMENT

Evaluation Of Toxicology

The toxicological database for pyrithiobac-sodium which consists primarily of toxicity tests conducted using animals, is quite extensive. In interpreting the data, it should be noted that toxicity tests generally use doses which are high compared to likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes at which no adverse health effects in humans would be expected.

Toxicokinetics and Metabolism

In rats, pyrithiobac-sodium is completely absorbed after low oral doses (5 mg/kg), but a significant proportion is not absorbed after high doses (250 mg/kg). The chemical is rapidly excreted via urine and faeces (>90% within 48 hours). The percentage excreted in urine is greater in females than males. Tissue levels are low 120 hours after an oral dose, with the highest concentrations of pyrithiobac-sodium found in the kidneys, liver and blood.

Pyrithiobac-sodium is metabolised extensively with the main urinary and faecal metabolite resulting from O-demethylation of one of the methoxy substituents in the pyrimidine ring. Minor metabolites result from cleavage of the sulphur bridge of pyrithiobac-sodium, followed by conjugation with glucuronic acid and 5-hydroxylation of the pyrimidine ring of pyrithiobac-sodium. Metabolism is greater in males than in females.

Acute Studies

Pyrithiobac-sodium exhibits low acute oral (LD50 = 3,200 mg/kg, in rats), dermal (LD50 > 2,000 mg/kg, in rabbits) and inhalation (LC50 > 6,900 mg/m³, in rats) toxicity. Pyrithiobac-sodium is a slight irritant to rabbit eye. No skin irritation in rabbits or skin sensitisation in guinea pigs was observed.

The acute oral toxicity in rats of the end-use product, Du Pont Staple® Herbicide, containing 85% pyrithiobac-sodium, is low (LD50 = 4,000 mg/kg). Dermal and inhalation toxicities are low in rabbits (LD50 > 2,000 mg/kg) and rats (LC50 > 5,600 mg/m³), respectively. Du Pont Staple® Herbicide is a moderate irritant to the rabbit eye and skin. It did not produce skin sensitisation in guinea pigs.
Short-Term Studies

Application of 1,200 mg of pyrithiobac-sodium/kg/day for 22 days to rabbit skin resulted in dermal irritation characterised by erythema, oedema, epidermal scaling or thickening, superficial necrosis and fissuring, and skin inflammation often associated with hyperkeratosis and/or acanthosis.

During a 90 day mouse feeding study, males receiving 1,241 mg of pyrithiobac-sodium/kg/day showed a reduction in mean body weight gain. Reductions in platelet and various white cell parameters were noted in male and female mice fed between 263 and 1,668 mg/kg/day. Increased liver weights, elevated hepatic peroxisomal β-oxidation, and enlarged liver cells were noted in males and females fed 1,241 or 1,668 mg of pyrithiobac-sodium/kg respectively.

In a 90-day rat feeding study, there was a reduction in male bodyweight gain, anaemia, and a reduction in serum triglyceride concentration at doses ranging from 466 to 1,609 mg of pyrithiobac-sodium/kg/day. There was a reduction in serum total protein and globulin in males fed doses from 3 to 1,376 mg/kg/day. Increased liver weights and hepatocellular hypertrophy (minimal to mild) was seen in male rats fed 466 and 1,376 mg of pyrithiobac-sodium/kg/day, and female rats fed 1,609 mg/kg/day. Hepatic β-oxidation rate was increased in males and females fed 1,376 or 1,609 mg of pyrithiobac-sodium/kg/day respectively, and cytochrome P-450 content was increased at male rats at doses ranging from 32 mg to 1,376 mg/kg/day.

Amongst dogs which were fed 618 mg of pyrithiobac-sodium/kg/day for 13 weeks, males showed an early reduction in bodyweight, which returned to normal after 2 weeks. Females showed anaemia at a dose of 633 mg/kg/day. Increased liver weights were noted in males and females at doses of 618 and 633 mg of pyrithiobac-sodium/kg/day, but pathology was unaffected.

Long-Term Studies

A reduction in mean weight gain, and a minor reduction in the white blood cell count was seen in male and female mice fed 745 and 1,101 mg of pyrithiobac-sodium/kg/day respectively for 18 months. An increase in the incidence of altered liver structure was noted in males receiving 745 mg/kg/day. In addition, there was an increase in the incidence of glomerulonephropathy in males and females fed 745 and 1,101 mg of pyrithiobac-sodium/kg/day respectively. The occurrence of hepatic adenoma in males receiving 217 mg of pyrithiobac-sodium/kg/day was significantly elevated.

Survival of rats fed a dietary source of 0.2 to 918 mg of pyrithiobac-sodium/kg/day for 2 years ranged from 30-53%. A significant decrease in body weight gain was noted in females receiving 918 mg/kg/day. After 6 to 12 months, females receiving 278 or 918 mg of pyrithiobac-sodium/kg/day showed signs of anaemia and/or reduced white blood cell count, and males being fed 200 mg/kg/day showed evidence of anaemia. Kidney disease was seen in male and female rats receiving between 200 and 918 mg of pyrithiobac-sodium/kg/day respectively, and kidney pathology was noted.
in females fed 918 mg/kg/day. After 2 years, liver pathology, and an increased incidence of renal tubular adenomas were noted in male and female rats fed 200 and 918 mg/kg/day respectively. The occurrence of renal tubular adenocarcinomas in males receiving 200 mg of pyrithiobac-sodium/kg/day was increased.

Signs of anaemia, and an increase in thyroid with parathyroid weight, and liver weights were evident in male and female Beagle dogs that were fed dietary levels of 580 and 647 mg of pyrithiobac-sodium/kg/day respectively for 52 weeks. An increase in lipofuscin was noted in the liver of males and females receiving 580 or 647 mg/kg/day respectively, and the kidney of females receiving 647 mg/kg/day.

Reproduction and Developmental Studies

In a one generation dietary reproduction study, mean offspring weights were reduced in a group in which the females received 1,609 mg of pyrithiobac-sodium/kg/day for 93 days before mating and throughout the reproduction period. Toxicity in adult animals receiving 1,376 (males) or 1,609 (females) mg/kg/day was seen as a reduction in bodyweight gain.

In a two generation dietary reproduction study, pup weights were reduced at maternal doses of 624 and 1,831 mg of pyrithiobac-sodium/kg/day. Toxicity in adult animals was observed as reduced bodyweight gain and food consumption at the same dose rates.

A developmental toxicity study was performed in which pyrithiobac-sodium was administered by gavage to rats on days 7-16 of gestation. Evidence of maternal toxicity at 1,800 mg/kg/day was seen as increased mortality, enlarged spleens and extramedullary haematopoesis of the spleen, reduced bodyweight gain and reduced food consumption, with increased incidence of staining of the fur in the perineal, inguinal and abdominal areas also observed at 600 mg/kg/d. Treatment-related effects on the foetus at 1,800 mg/kg/day included an increased incidence of foetuses with minor developmental variations, specifically due to an increase in the presence of rudimentary cervical ribs.

A developmental toxicity study was performed in rabbits with doses of pyrithiobac-sodium administered orally on days 7-19 of gestation. Maternal toxicity at 1,000 mg/kg/day included increased mortality, increased tail staining and diarrhoea and reduced bodyweight gain and food consumption. There was an increase in embryo death, and foetal weight was reduced at 1,000 mg/kg/day. Pyrithiobac-sodium was not teratogenic in this study.

Genotoxicity

Pyrithiobac-sodium did not exhibit mutagenicity in S. typhimurium and E. coli, and did not induce DNA damage in rat hepatocytes. The chemical was tested for chromosome damage in two in vivo mouse bone marrow micronucleus studies, over an oral dose range of 500-3,000 mg/kg, and was not genotoxic in either study.
Pyrithiobac-sodium showed ability to damage chromosomes in cultured human lymphocytes. In an in vitro chromosomal aberration test in Chinese hamster lung cells, pyrithiobac-sodium at high concentrations (1,300, and 2,600 μg/mL) in the absence, and at 5,400 μg/mL in the presence, of metabolic activation, slightly increased aberrant cell frequencies. The weight of evidence indicates that pyrithiobac-sodium is not a genotoxic agent.

**Conclusion**

Based on an assessment of the toxicology, it was considered that no adverse effects on human health would be expected when the product is used in accordance with label directions.

**PUBLIC HEALTH STANDARDS**

**Poisons Scheduling**

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients and assessed the necessary controls to be implemented under States' poisons regulations to prevent the occurrence of poisoning.

The NDPSC recommended that pyrithiobac-sodium be listed in Schedule 5 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the label.

**No Observable Effect Level (NOEL) and Acceptable Daily Intake (ADI)**

The most sensitive species was the mouse, with a NOEL of 21 mg/kg/day. In order to calculate the acceptable daily intake for humans, a safety factor is applied to the NOEL in the most sensitive species. The magnitude of the safety factor is selected to account for uncertainties in extrapolation of animal data to humans; variation within the human population; the quality of the experimental data; and the nature of the potential hazards. Using a safety factor of 100, an ADI of 0.2 mg/kg/day for pyrithiobac-sodium was established.

**Potential for Chemical Residues in Food**

**Background**

Appropriate residue and metabolism studies were provided, in accordance with the Requirements for Clearance of Agricultural and Veterinary Chemical Products, to support the use of pyrithiobac-sodium on cotton in Australia. This data was reviewed by chemical residues reviewers in the NRA.
Residues In Food Commodities

Residue data were presented for cotton, cotton seed and the processed cotton seed oils, from trials conducted in Australia and overseas.

Cotton seed and forage

Trials were conducted with two treatments at rates equivalent to, and up to four times the maximum recommended rate i.e. 100 – 400 g ai/ha. Residues in cotton seed at the proposed withholding period of 63 days were at the limit of determination, ≤ 0.005 mg/kg, or not detectable at all. Residues in cotton forage were approximately 0.2 mg/kg, 35 days after treatment.

Processed fractions

Residues of pyrithiobac-sodium in cotton were just detectable at 0.006 mg/kg, after 2 treatments at 3.5 times the maximum recommended rate.

In lint, cotton seed, delinted seed, crude oil, meal, refined oil, cotton seed hulls and soap stock, residues were not detected.

The residue data indicate that, in accordance with the recommended pattern of use, the following withholding period is appropriate:

Cotton – 9 weeks before harvest, grazing or cutting for stock feed

Metabolism studies conducted on cotton plants in the U.S.A., indicated that in addition to the parent compound, two metabolites were formed, the O-desmethyl derivative and its glucose conjugate. At the proposed withholding period of 63 days, the parent compound had been completely metabolised; at 77 days all metabolites (residues) are at the limit of detection.

Animal metabolism studies were conducted in rats, hens and goats. Up to 90% of the pyrithiobac-sodium was excreted in all species, and the remaining residue was composed of the parent compound and one metabolite, the O-desmethyl derivative. In the lactating goat, no detectable residues were found in milk or meat; small amounts of residue were located in the kidney and liver, however these were at or below the limit of detection.

Detailed descriptions of the analytical method were provided. The major metabolites were determined as the parent compound, which was directly measured using GC-MS. The limits of determination ranged from 0.005 – 0.01 mg/kg.
MRL STANDARD

The following additions to the MRL Standard have been recommended:

Table 1
Maximum residue limits of pesticides, agricultural chemicals, veterinary medicines and associated substances in food commodities

<table>
<thead>
<tr>
<th>Compound (mg/kg)</th>
<th>Food</th>
<th>MRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrithiobac-sodium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SO 0691</td>
<td>Cotton seed</td>
<td>*0.01</td>
</tr>
<tr>
<td>OC 0691</td>
<td>Cotton seed oil, crude</td>
<td>*0.01</td>
</tr>
<tr>
<td>OR 0691</td>
<td>Cotton seed oil, edible</td>
<td>*0.01</td>
</tr>
<tr>
<td>MM 0095</td>
<td>Meat (mammalian)</td>
<td>T*0.01</td>
</tr>
<tr>
<td>MO 0105</td>
<td>Edible offal (mammalian)</td>
<td>T*0.01</td>
</tr>
<tr>
<td>ML 0106</td>
<td>Milks</td>
<td>T*0.01</td>
</tr>
<tr>
<td>PO 0111</td>
<td>Poultry, edible offal of</td>
<td>*0.01</td>
</tr>
<tr>
<td>PM 0110</td>
<td>Poultry meat</td>
<td>*0.01</td>
</tr>
<tr>
<td>PE 0112</td>
<td>Eggs</td>
<td>*0.01</td>
</tr>
</tbody>
</table>

Table 4
Recommended maximum residue limits for pesticides in animal feed commodities

<table>
<thead>
<tr>
<th>Compound</th>
<th>Animal Feed Commodity</th>
<th>MRL (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrithiobac-sodium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV 0691</td>
<td>Cotton forage</td>
<td>T0.2</td>
</tr>
</tbody>
</table>
OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Occupational health and safety data provided in support of registration of DuPont Staple Herbicide was reviewed by Worksafe Australia.

Pyritzhiobac-sodium is determined not to be a hazardous substance by Du Pont (Australia) Ltd according to National Occupational Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances.

DuPont Staple Herbicide is determined to be a hazardous substance by Du Pont (Australia) Ltd, according to NOHSC Criteria because of the degree of eye irritation observed in animals.

DuPont Staple Herbicide is a water soluble powder formulation contained within pre-measured water soluble bags. It will be imported fully formulated in water soluble bags and re-packaged into sales packs in Australia.

Pyritzhiobac-sodium and DuPont Staple Herbicide are not classified as dangerous goods under the Australian Code for the Transport of Dangerous Goods by Road and Rail.

Re-packaging, transport, storage and retailing

Australian workers involved in the re-packaging of water soluble bags into 1.2 kg sales packs should be protected by safe work practices, an enclosed packaging process, ventilation and training commensurate with risks identified in the workplace assessment. Where handling processes are not contained, workers should wear personal protective equipment.

Australian workers involved in transport, storage and retailing of the product are unlikely to be exposed to the product unless the packaging is breached.

Advice on the safe handling of the product during routine transport and storage is provided on the Material Safety Data Sheet (MSDS) for DuPont Staple Herbicide.

End use

DuPont Staple Herbicide may be applied by ground or aerial spray, to control certain broadleaf weed control in cotton. It may be used by owner operators or contract workers.

End users may become contaminated with DuPont Staple Herbicide when making up the working strength solution and applying the spray. The concentration of product in the spray will be ≤ 0.12% for ground application and ≤ 0.4% for aerial application. Workers will also need to clean up spills and maintain and clean spray equipment.

The product is of low acute toxicity. It is an eye and skin irritant.
Workers diluting the product will not directly handle the concentrate, so the potential for contamination is much reduced. Contamination with the working strength solution on the skin or by inhalation of spray mist is not expected to result in short-term or long-term health effects in end users. Specific personal protective clothing is not considered necessary for workers diluting the product or spraying the working strength solution. All workers should adopt good occupational hygiene practices.

End users should follow the directions on the DuPont Staple Herbicide label. Safety directions on the label caution workers to avoid contact with eyes and skin and to wash eyes and skin immediately if contaminated with the product. The label also cautions users not to excessively handle the water soluble bags and to ensure they remain dry before use. End users should refer to the product MSDS for additional information.

**Entry into treated areas**

The product is designed to reduce the need for manual weeding in cotton crops. In the event that cotton chippers or crop checkers need to re-enter treated fields, the low vapour pressure, low application rate for the product and its toxicity profile suggest that entry into treated fields does not pose any occupational health and safety concern.

**Recommendations for safe use - all workers**

Workers involved in re-packaging should be protected by engineering controls such as exhaust ventilation, safe work practices and training. Where handling process are not fully contained workers should wear long sleeved overalls (AS 3765-1990 Clothing for protection against hazardous chemicals), approved safety boots (AS/NZS 2210.2-1994 Occupational protective footwear), safety glasses (AS/NZS 1337-1992 Eye protectors for industrial applications) and PVC or nitrile rubber gloves (AS 2161-1978 Industrial safety gloves and mittens).

End users should follow the safety directions on the DuPont Staple Herbicide label. Specific personal protective equipment is not prescribed for this product. However, the safety directions advise users to avoid contact with eyes and skin and wash them immediately if contaminated with the product.

**Conclusion**

DuPont Staple Herbicide can be used safely if handled in accordance with the control measures described above. Additional information is available on the label and in the MSDS.
TRADE ASSESSMENT

DuPont Staple Herbicide is currently registered in the U.S.A., Columbia and Venezuela specifically for use on cotton.

The US has set a tolerance of 0.02 ppm which is twice the Australian MRL of 0.01 ppm. Currently there have been no Codex MRLs set for pyrithiobac-sodium.

The residue data presented show that residues in cotton produce decline to below the limit of detection; therefore residue detection in exported commodities is unlikely. MRLs in food commodities in Australia have all been set at the limit of detection, no finite residues could be detected.

The chemical is highly water soluble and therefore would not partition into fat and would not be expected to accumulate in fatty tissues in livestock.

Conclusion

Du Pont Staple Herbicide is not expected to have an impact on Australia’s trade with other nations.
<table>
<thead>
<tr>
<th>Glossary of terms:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active constituent</strong></td>
</tr>
<tr>
<td>The component of a treatment which is responsible for its biological effect.</td>
</tr>
<tr>
<td><strong>Acute toxicity</strong></td>
</tr>
<tr>
<td>Immediately measurable effects of a toxin on an organism.</td>
</tr>
<tr>
<td><strong>Denatured</strong></td>
</tr>
<tr>
<td>Broken down</td>
</tr>
<tr>
<td><strong>Detritus</strong></td>
</tr>
<tr>
<td>Rotting vegetable material</td>
</tr>
<tr>
<td><strong>Diploid</strong></td>
</tr>
<tr>
<td>Having two sets of chromosomes</td>
</tr>
<tr>
<td><strong>DNA</strong></td>
</tr>
<tr>
<td>Deoxyribonucleic acid the generic component of the chromosomes which support the gene sequences.</td>
</tr>
<tr>
<td><strong>Gene</strong></td>
</tr>
<tr>
<td>A length of the DNA which holds the base sequences which code for the formation of a polypeptide chain (protein).</td>
</tr>
<tr>
<td><strong>IPM</strong></td>
</tr>
<tr>
<td>Integrated Pest Management. The combination of chemical and biological aspects of pest control to achieve pest management.</td>
</tr>
<tr>
<td><strong>ppm</strong></td>
</tr>
<tr>
<td>Parts per million</td>
</tr>
<tr>
<td><strong>Protease</strong></td>
</tr>
<tr>
<td>Enzymes which break down proteins.</td>
</tr>
<tr>
<td><strong>Proteolysis</strong></td>
</tr>
<tr>
<td>The process in which proteins chains are lysed (cut) as part of their digestion.</td>
</tr>
<tr>
<td><strong>Schedule</strong></td>
</tr>
<tr>
<td>The category into which a chemical is placed according to its human toxicity.</td>
</tr>
</tbody>
</table>
SUGGESTED FURTHER READING

*Code of Practice for Labelling Agricultural Chemical Products* (available from the NRA)


*Interim Requirements for the Registration of Agricultural and Veterinary Chemical Products* (available from the NRA)

*MRL Standard - Maximum residue limits in food and animal feedstuffs.*
Commonwealth Department of Human Services and Health. AGPS, Canberra.

Primary pack

CAUTION
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Staple®
herbicide

ACTIVE CONSTITUENT: 850 g/kg PYRITHIOBAC-SODIUM

GROUP B HERBICIDE

For the control of certain broadleaf weeds in Cotton as per Directions for Use table.

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USE

PRIMARY PACK CONTAINS 10 x 120 g MEASURE PACKS ENCLOSED IN A WATERPROOF BAG WHICH IT IS ILLEGAL TO SELL SEPARATELY. THE BAG WITH UNUSED MEASURE PACKS MUST BE RETURNED TO THE OUTER PACK AFTER USE. DO NOT DESTROY OUTER PACK WHILE PRODUCT REMAINS

NET 1.2 kg

Du Pont (Australia) Limited
A.C.N. 000 716 469
168 Walker Street, North Sydney NSW 2060

© DuPont Registered Trademark
STORAGE AND DISPOSAL

Keep from contact with fertilisers, other pesticides and seeds.
Store in closed, original container in a dry, well-ventilated area, as cool as possible out of direct sunlight.
DO NOT store in or expose product to wet conditions. Rough handling of product may cause breakage of water soluble bags, especially at low temperatures.
Puncture and bury in a local authority landfill or below 500 mm depth at an approved disposal site clear of waterways and vegetation roots, (check State regulations). DO NOT burn empty containers or product.

SAFETY DIRECTIONS

Will irritate the eyes and skin. Avoid contact with eyes and skin. If product in eyes, wash it out immediately with water. If product on skin wash wash area with soap and water. Wash hands after use.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre.

For further information refer to the Material Safety Data Sheet.

NOTICE TO BUYER

To the extent permitted by law all conditions and warranties and statutory or other rights of action which buyer or any other user may have against DuPont or Seller are hereby excluded. DuPont hereby gives notice to buyer and other users that it will not accept responsibility for any indirect or consequential loss arising from reliance on product information or advice provided by DuPont or on its behalf unless it is established that such information or advice was provided negligently and that the product has been used strictly as directed. DuPont's liability shall in all circumstances be limited to replacement of the product or a refund of the purchase price paid therefor.

Batch No.:
Date of Manufacture:  
NRA Approval No.: 46441/1
CAUTION
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Staple®
herbicide

ACTIVE CONSTITUENT : 850 g/kg PYRITHIOBAC-SODIUM

MEASURE ONLY - ILLEGAL TO BE SOLD EXCEPT IN UNOPENED PRIMARY PACK
BEFORE USE READ ALL DIRECTIONS ON THE LABEL OF THE PRIMARY
WATER SOULBLE PACKAGING. KEEP DRY

120 g

Du Pont (Australia) Limited
A.C.N. 000 716 469
168 Walker Street, North Sydney NSW 2060

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CAUTION
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

STAPLE®
herbicide

ACTIVE CONSTITUENT: 850 g/kg PYRITHIOBAC-SODIUM

THIS WATERPROOF BAG CONTAINS 10 WATER SOLUBLE MEASURE PACKS. BEFORE USE READ DIRECTIONS ON THE OUTER PACK. KEEP UNUSED MEASURE PACKS IN THIS BAG AND RETURN TO OUTER PACK AFTER USE OR DISPOSE OF IN ACCORDANCE WITH THE LABEL DIRECTIONS. SALE OF THIS BAG EXCEPT IN OUTER PACK IS ILLEGAL.

Du Pont (Australia) Limited
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168 Walker Street, North Sydney NSW 2060

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CAUTION
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING

DUPONT

Staple®
herbicide

ACTIVE CONSTITUENT: 850 g/kg PYRITHIOBAC SODIUM

GROUP B HERBICIDE

COMPLETE DIRECTIONS FOR USE

Du Pont (Australia) Limited
A.C.N. 000 716 469
168 Walker Street, North Sydney NSW 2060

® DuPont Registered Trademark

DuPont Staple® herbicide draft label

Issued: 18/3/96
Replaces: 8/2/96
DIRECTIONS FOR USE
RESTRAINTS
DO NOT apply DuPont Staple® herbicide to cotton growing under stress caused by severe weather conditions (such as drought or waterlogging), insects or disease as crop injury may occur.
DO NOT apply to weeds that are stressed by any cause (such as weather conditions, drought, waterlogging) or not actively growing. Weeds under stress are less susceptible to herbicide activity. This may result in an incomplete kill or suppression of weeds only.
DO NOT store spray preparations of DuPont Staple herbicide for more than 24 hours, as product breakdown may occur.
DO NOT store tank mixes of DuPont Staple herbicide.
DO NOT apply if rainfall is expected within 4 hours.
DO NOT APPLY COTTON FOR 9 WEEKS AFTER APPLICATION.

APPROPRIATE LEGISLATION.

NOT TO BE USED FOR ANY PURPOSE OR IN ANY MANNER CONTRARY TO THIS LABEL UNLESS AUTHORIZED UNDER

<table>
<thead>
<tr>
<th>Crop</th>
<th>Critical Comments</th>
<th>Application Rate</th>
<th>Minimum Weed Stage</th>
<th>Dose Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotton</td>
<td>Yellow vine</td>
<td>60 - 90 g a.i.</td>
<td>Up to 15 cm in diameter</td>
<td>60 g a.i.</td>
</tr>
<tr>
<td></td>
<td>(Triumficus microrrhizus)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wild Meron</td>
<td>120</td>
<td>Up to 2 leaf stage</td>
<td>120 g a.i.</td>
</tr>
<tr>
<td></td>
<td>(Helianthus annuus)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Volunteer Sunflower</td>
<td>30</td>
<td>Up to 6 leaf stage</td>
<td>30 g a.i.</td>
</tr>
<tr>
<td></td>
<td>Sunflower</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Trampolite</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(S. benedictiana)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Sesbania canadensis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sesbania</td>
<td>60 - 90</td>
<td>Up to 5 cm in height</td>
<td>60 g a.i.</td>
</tr>
<tr>
<td></td>
<td>(Polyphora assimilis)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Polyphora</td>
<td>90</td>
<td>Up to 6 leaf stage</td>
<td>90 g a.i.</td>
</tr>
<tr>
<td></td>
<td>(Chamaelea litigiosa)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Nogoodour</td>
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<tr>
<td></td>
<td>(Commoneon phanthere)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bogbean weed</td>
<td>120</td>
<td>Up to 2 leaf stage</td>
<td>120 g a.i.</td>
</tr>
<tr>
<td></td>
<td>(Arumaria minor)</td>
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<tr>
<td></td>
<td>(Bullhornb)</td>
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<tr>
<td></td>
<td>(Irritealess pedea)</td>
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<tr>
<td></td>
<td>Bellbine</td>
<td>60</td>
<td>Up to 15 cm diameter or</td>
<td>60 g a.i.</td>
</tr>
<tr>
<td></td>
<td>(Chamaelea spinosa)</td>
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<tr>
<td></td>
<td>English Birt</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(Rana colorata)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Weed weed</td>
<td>120</td>
<td>Up to 2 leaf stage</td>
<td>120 g a.i.</td>
</tr>
<tr>
<td></td>
<td>(Pyrethris angustifol)</td>
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<td></td>
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<tr>
<td></td>
<td>(Annual Ground Cherry)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Cotton</td>
<td></td>
<td></td>
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</tbody>
</table>
GENERAL INSTRUCTIONS

Post-emergence application of DuPont Staple® herbicide may be made from the first true leaf stage to early flowering. Application may be made to both irrigated and dryland cotton crops. For best results apply when soil is moist and weeds are actively growing.

DuPont Staple herbicide may be applied more than once in the same season if the crop shows no sign of previous injury. In cases where it is necessary to apply a second spray in that season, the total amount of product should not exceed 240 g/ha when intending to plant back to cotton, or 120g/ha when intending to plant other crops after the season. Refer to Crop Rotation Recommendations for more information.

DuPont Staple herbicide is absorbed by foliage and to some extent taken up by roots. Herbicide symptoms on susceptible weeds appear within 5-10 days of application.

Resistant Weeds Warning

DuPont Staple herbicide is a member of the benzoate group of herbicides. DuPont Staple herbicide has the Inhibitor of Acetolactate Synthase (ALS) mode of action. For weed resistance management DuPont Staple herbicide is a Group B herbicide.

Some naturally-occurring weed biotypes resistant to DuPont Staple herbicide and other ALS herbicides may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by DuPont Staple herbicide or other ALS herbicides.

Since the occurrence of resistant weeds is difficult to detect prior to use, DuPont accepts no liability for any losses that may result from failure of DuPont Staple herbicide to control resistant weeds.

Large numbers of healthy surviving weeds can be an indication that resistance is developing. Efforts should be taken to prevent seed set of these survivors.

Avoid the prolonged use of ALS inhibitor herbicides on the same weed population.

If the user suspects that an ALS inhibitor resistant weeds are present, DuPont Staple herbicide or other ALS inhibitors herbicides recommended for the control of that weed should not be used.

Strategies to minimise the risk of herbicide resistance are available. Consult your farm chemical supplier, consultant, local Department of Agriculture or Primary Industries, or local DuPont Representative.

Crop Safety

DuPont Staple herbicide may cause temporary injury to cotton (expressed as leaf yellowing and/or biomass reduction).

Spray Preparation

DuPont Staple herbicide is a water soluble powder formulation and is contained within a water soluble bag. The water soluble bags dissolve readily in water. DO NOT excessively handle water soluble bags or expose to moisture because this may cause breakages. DO NOT touch bags with wet hands or place on wet surfaces. Protect unused bags by resealing in original container.

Partially fill the spray tank with water. Add the required number of water soluble bags to the spray tank with the agitation system engaged. Top up to the correct volume of water. Continuous agitation is required for uniform application. Where prepared spray solution has been allowed to stand, thoroughly agitate before use.

When tank mixed with other herbicides add DuPont Staple herbicide into the spray tank BEFORE adding companion herbicides and surfactant.

Decontaminate spray equipment before using DuPont Staple herbicide if it was used to spray herbicides other than DuPont Staple herbicide or MSMA. Follow cleaning procedure provided on the relevant product label, if that is not available refer to section "Sprayer Cleanup" on this label and follow steps 1 to 6.
Use of Surfactant/Wetting Agent
Always add a non-ionic surfactant at the rate of 0.25 % v/v of final spray volume (i.e. 250 mL/100 L of a 1000 g/L product)
DO NOT use spraying oils with DuPont Staple® herbicide, as excessive crop injury may occur.

Application Information
DuPont Staple herbicide may be applied as a post-emergent band or directed spray or as a (over the top) blanket spray. In certain situations it is preferable to use blanket spraying (see below)

Post-emergent applications should be made to young actively growing weeds. Calibrate spray equipment to a constant ground speed and rate of delivery to ensure thorough coverage and uniform spray pattern. The droplet size to be achieved in all applications of Staple is between 200-250μm. Apply DuPont Staple herbicide in a minimum of 100 L of water per sprayed hectare and follow instructions on companion herbicide label when tank mixing with other products.

Band Spraying (over the top)
Spray nozzles should be mounted on droppers at approx. 25 cm either side of the cotton row (i.e. 2 nozzles per row) and at a height above the crop to accurately spray the desired band width (e.g. 40 cm). The recommended nozzle types for this configuration are 80° flat fan or 80° hollow cone nozzles.

Directed Spraying (under canopy)
When crop canopy prevents good penetration or when DuPont Staple herbicide is tank mixed with other herbicides (lay-by application) use directed sprays.

Blanket Spraying
In the following situations blanket spraying using 110° flat fan nozzles is the most effective method of application:

i) when controlling 20-50 cm high Sesbania using either high clearance ground rigs or aircraft

ii) when controlling populations of Datura sp. at 6-8 true leaf stage, Amaranthus spp. and Tribulus spp. 5 cm or larger in diameter or Polymeria spp. at 6 true leaf stage.

Aerial Spraying
DuPont Staple herbicide may only be applied by air as a salvage treatment for Sesbania Pea (Sesbania cannabina, S. benthamiana). Apply in a minimum of 30 L/ha water. Avoid spraying in still conditions and in winds likely to cause drift onto adjacent sensitive crops or fallow areas likely to be planted to these crops. Turn off spray boom whilst passing over creeks, dams, channels and rivers. DO NOT apply when a temperature inversion is likely to occur.

Cultivation
Do NOT cultivate immediately before or within 7 days after application.
Sprayer Cleanup

Spray equipment must be clean and free of previous pesticide deposits before applying DuPont Staple herbicide and properly cleaned out after use. Use the cleanup procedures specified on the label of the previously used product, clean all application equipment before applying DuPont Staple herbicide. If no cleanup procedure are provided, use the following procedure. Immediately following applications of DuPont Staple herbicide thoroughly clean all mixing and spray equipment according to the following instructions:

1. Drain Tank: Thoroughly hose down the interior surfaces of the tank; then flush tank, boom and hoses with clean water for a minimum of 5 minutes. Loosen and physically remove any visible deposits.

2. Fill the tank with clean water and add 1 L of household ammonia* (3% active) for every 100 L. of water. Flush the cleaning solution through the boom, hoses and nozzles. Add more water to completely fill the tank and allow to agitate/recirculate for at least 15 minutes. Again, flush the boom, hoses and nozzles with the cleaning solution, then drain the tank.

3. Remove the nozzles and screens and clean separately in a bucket containing the cleaning agent and water.

4. Repeat step 2.

5. Thoroughly rinse the tank with clean water for a minimum of 5 minutes, flushing the water through the hoses and boom.

6. Dispose of the rinsate on site or at an approved waste disposal facility.

* Equivalent amounts of an alternate-strength ammonia solution or DuPont approved cleaner can be used in the cleanout procedure. Carefully read and follow the individual cleaner instruction.

CAUTION: DO NOT use chlorine bleach with ammonia when cleaning out spray tanks. All traces of liquid fertiliser containing ammonia, ammonia nitrate or ammonium sulphate must be rinsed with water from the mixing and application equipment before adding any chlorine bleach solution. Failure to do so will release a gas with a musty chlorine odour which can cause eye, nose, throat and lung irritation. DO NOT clean equipment in an enclosed area.

Compatibilities
DuPont Staple herbicide is compatible with the commonly used cotton herbicides: MSMA, Karmex® F, Karmex® DF™, Prometryn and Fluometuron and insecticides Folim 800, Lannate® L, Endosulfan. DuPont Staple herbicide is incompatible with DuPont Targa® herbicide.

When tankmixing DuPont Staple herbicide also add a non-ionic surfactant at a rate of 0.25 % v/v of final spray volume (i.e. 250 mL/100 L of a 1000 g/L product).

Crop Rotation Recommendations:
DuPont Staple herbicide is broken down primarily by microbial degradation. Soils low in organic matter may slow down the breakdown of DuPont Staple herbicide.

Cultivate land treated with DuPont Staple herbicide before rotational crop is planted.

Land treated with DuPont Staple herbicide should not be rotated to crops other than those listed below:

<table>
<thead>
<tr>
<th>CROP</th>
<th>INTERVAL (MONTHS)</th>
<th>MAXIMUM PRODUCT USED PER SPRAYED HECTARE g/ha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotton</td>
<td>0 (no restriction)</td>
<td>240</td>
</tr>
<tr>
<td>Barley</td>
<td>5</td>
<td>120</td>
</tr>
<tr>
<td>Oats</td>
<td>5</td>
<td>120</td>
</tr>
<tr>
<td>Wheat</td>
<td>5</td>
<td>120</td>
</tr>
<tr>
<td>Maize</td>
<td>22</td>
<td>120</td>
</tr>
<tr>
<td>Sorghum(grain)</td>
<td>22</td>
<td>120</td>
</tr>
<tr>
<td>Soybeans</td>
<td>22</td>
<td>120</td>
</tr>
<tr>
<td>Sunflower</td>
<td>22</td>
<td>120</td>
</tr>
</tbody>
</table>
Tolerance of crops not listed in the table should be determined using field bioassay (small scale test strip grown through to maturity).

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS

Injury to or loss of desirable crops, vegetation, aquatic plants, or trees may result from failure to observe the following:

DO NOT apply irrigation tailwaters to crops other than cotton, or release tailwaters to drains or waterways.

DO NOT apply or drain or flush equipment on or near desirable trees or other plants or on areas where their roots may extend or in locations where the chemical may be washed or moved into contact with their roots.

DO NOT apply or allow spray to drift onto adjacent crops and non-target desirable plants, or onto agricultural land scheduled to be planted to other crops as injury to the crop may occur.

PROTECTION OF WILDLIFE, FISH, CRUSTACEA AND ENVIRONMENT

DO NOT contaminate any body of water by spraying, cleaning of equipment or disposal of waste.

STORAGE AND DISPOSAL

Withhold irrigation as long as possible after application according to company advice on timing of application and irrigation.

Keep from contact with fertilisers, other pesticides and seeds.

Store in closed, original container in a dry, well-ventilated area, as cool as possible out of direct sunlight.

DO NOT store in or expose product to wet conditions. Rough handling of product may cause breakage of water soluble bags, especially at low temperatures.

Puncture and bury in a local authority landfill or below 500 mm depth at an approved disposal site clear of waterways and vegetation roots, (check State regulations). DO NOT burn empty containers or product.

SAFETY DIRECTIONS

Will irritate the eyes and skin. Avoid contact with eyes and skin. If product in eyes, wash it out immediately with water. If product on skin wash wash area with soap and water. Wash hands after use.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre.

For further information refer to the Material Safety Data Sheet.

NOTICE TO BUYER

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