National Registration Authority
For Agricultural & Veterinary Chemicals

The NRA Review of

TRIFORINE
(aqueous formulations)

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FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent statutory authority with responsibility for the regulation of agricultural and veterinary chemicals. One of the NRA's regulatory responsibilities is to review registered agricultural and veterinary chemicals to ensure that they are effective and that they do not pose unacceptable risks to people, the environment or Australia's export trade.

When reviewing agricultural and veterinary chemicals, the NRA works in close co-operation with advisory agencies including the Department of Health and Aging (TGA), Environment Australia (Risk Assessment and Policy Section), National Occupational Health and Safety Commission (Agricultural and Veterinary Chemicals Section) and State Departments of Agriculture.

The NRA has a policy of encouraging openness and transparency in its activities and community involvement in decision-making. When the NRA decides to conduct a review, it often consults parties that might be affected by the review (such as registrants, commodity groups, State regulatory agencies) and invites submissions regarding the concerns of the review. All participants are notified of the NRA's decision(s), which are also published in the NRA's Agricultural and Veterinary Chemicals Gazette.

The review report provides an overview of the NRA's review. The review findings can be based on information collected from a variety of sources, including data packages and information submitted by registrants, information submitted by members of the public and government organisations, as well as literature searches.

The NRA makes these reports available to the public and regulatory agencies of other countries that are part of the OECD *ad hoc* exchange program and as part of bilateral exchange agreements with other countries. Under the OECD *ad hoc* exchange program, it is proposed that countries receiving these reports will not utilise them for registration purposes unless they are also provided with the raw data from the relevant applicant.

The information and technical data required by the NRA to review the safety and effectiveness of both new and existing chemical products must be derived according to accepted scientific principles, as must the methods of assessment undertaken. Details of required data are outlined in various NRA publications (www.nra.gov.au).

ABBREVIATIONS AND ACRONYMS

ACA	Australian Consumer's Association
g	gram
L	litre
NRA	National Registration Authority for Agricultural and Veterinary Chemicals
pH	a measure of acidity or alkalinity
UV	ultra-violet

TABLE OF CONTENTS

1. INTRODUCTION

1.1 PRODUCT DESCRIPTIONS

Triforine products have been used as fungicides for approximately 30 years. Triforine is absorbed by the leaves and roots and then translocates upwards through the plant.[1] In the home garden, triforine products are used to control black spot, powdery mildew and rust on roses.

Triforine products were first registered in the State-based registration system in the 1970s. They were supplied as either concentrate or 'ready-to-use' formulations. Concentrates typically have an alcohol solvent and are diluted in water just prior to spraying. When the review commenced, however, two registered concentrates had water as their solvent. These two products were subject to the review as discussed in this report. Ready-to-use products had water as their solvent, having been diluted at the point of manufacture rather than just prior to spraying.

In this report, "products containing triforine in aqueous solution" means a product where the active constituent is triforine and the solvent is water.

1.2 REASONS FOR REVIEW

The NRA decided to review products containing triforine in aqueous solution to determine whether it could be satisfied that the continued use of these products in accordance with their label instructions (see Section 3) would be effective and thus whether their registrations and associated label approvals should be reconsidered.

The effectiveness of products containing triforine in aqueous solution depends on, among other things, the respective concentration of their active constituent and the rate of application specified on their approved label(s). A reduction in either of these parameters can cause a product to be ineffective. Products containing triforine at levels below the label declaration suggests that such products might not be effective and therefore not meet a criterion for continued registration (see Section 2).

The NRA's decision to review was based on information that was provided to it by the Australian Consumer's Association (ACA)[2] as well as information collected independently by the NRA. The information suggested that products containing triforine in aqueous solution might be unstable. That is, the triforine that they contain might degrade in water and become ineffective for its intended purpose. Section 1.3 discusses other actions taken by the NRA based on this information.

1.3 RELATED RECALL ACTION

The NRA took other actions beside the review that is the focus of this report. On receipt of the information provided by ACA, the NRA sought and received validation of the test methodology. At the same time, the NRA took samples of the products that are under review and had them analysed at the State Chemistry Laboratory (SCL) in Victoria.

[1] Tomlin, CDS. The Pesticide Manual. British Crop Protection Council, 2000: pp. 945 – 946.
[2] Australian Consumer's Association. Choice Magazine (Dec 2002): pp. 15 – 17

On the basis of the validated data provided by ACA and the NRA's data, the NRA undertook recall action. With the cooperation of the registrants of the products under review, all batches that were shown to contain triforine at levels below the amount declared on the label were recalled. Each registrant ceased supply of product into the market place.

1.4 PRODUCTS ORIGINALLY SUBJECT TO THE REVIEW

The products (and their associated approved labels) subject to the review at its commencement are listed in Table 1:

Table 1. Products and labels subject to the review

Product Number	Registrant	Product Name	Label Number(s)
40354	Yates	Yates Rose Gun Black Spot and Insect Killer	Ψ 40354/0902
42042	David Gray	David Grays Aerosol Rose Spray With Fungicide	Ψ 42042/01
48325	Ausgro	Ausgro Sharp Shooter Rose Black Spot and Timed Release Insect Spray	48325/01
49028	Ausgro	Sharp Shooter Triforine Rose Spray	49028/01 49028/0998
49029	Ausgro	Sharp Shooter Rose Black Spot & Natural Pyrethrum Concentrate	49029/01 49029/0898

Ψ Labels transitioned from the States and so not having an approval number

These products contain triforine in aqueous solution. The review did not focus on triforine products where the solvent is other than water.

1.5 CHANGES TO REGISTRATIONS SINCE COMMENCEMENT OF THE REVIEW

Before the review was completed, all three registrants requested that their respective registrations be cancelled. Being satisfied that there were no valid reasons not to do so, the NRA cancelled the registration of each product named in Table 1. Label approvals were also cancelled. Instructions for dealing with cancelled product are described in Section 5. Manufacturers are also recalling products from the market.

This report details the NRA's assessment of the stability and effectiveness of products containing triforine in aqueous solution and the recommendations arising from that assessment.

2 CRITERION FOR CONTINUED REGISTRATION

In the case of a chemical product that was registered by the NRA on the basis of being similar to a registered chemical product that was registered by the States at the commencement of the Agvet Codes, the matter of which the NRA must be satisfied is that the product contain the level of active constituent (in this case triforine) declared on the label that the NRA has approved.

If the NRA is not satisfied that the level of active constituent is not that declared on products label, the NRA may determine that the continued use of the product in accordance with its instructions for use would not be effective.

3. ASSESSMENT

3.1 CHEMISTRY

3.1.1 Chemical identity[3]

Common name: triforine

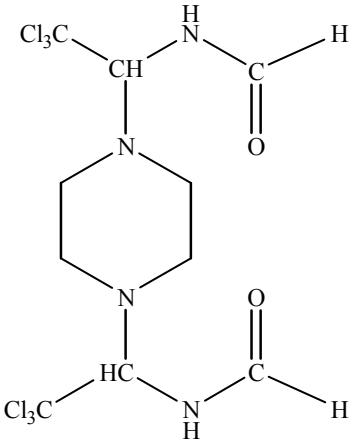
CAS name: N,N'-[1,4-piperazinediylbis(2,2,2-tricholroethylidene)]bisformamide

CAS number: 26644-46-2

Molecular formula: $C_{10}H_{14}Cl_6N_4O_2$

Molecular weight: 435.0

Structural formula:



3.1.2 Stability of triforine in aqueous solution

The recent ACA test results and the NRA's independently measured test results (which typically showed reductions in triforine of approximately 30% – 40% compared to the label claim) confirm other available scientific knowledge[4] that triforine is inherently unstable in aqueous solution. This is evident from its short half-life.

With regard to chemical degradation, the term "half-life" refers to the time in which a chemical will degrade to half its original concentration. Half-lives are independent of the starting concentration. For example, if a chemical has a half-life of 5 days (under certain conditions), then after 5 days (under those same conditions), a solution of the chemical that started at 100 g/L will have fallen to 50 g/L. Equally, a solution of the chemical that started at 40 g/L will have fallen to 20 g/L under the same conditions.

It appears to the NRA that triforine is hydrolysed in aqueous solution with a half-life of approximately 2 days at room temperature (*i.e.*, half of the triforine in aqueous solution is

[3] Tomlin, CDS. The Pesticide Manual. British Crop Protection Council, 2000: pp. 945 – 946.
[4] Darda, S, Darskus RL, Eichler R, Ost W and Wotschowkowsky M. Hydrolysis and photolysis of the fungicide triforine. Pesticide Science, 1977(8): pp. 183 – 192.

decomposed by hydrolysis after 2 days), with various polar degradation products formed as a result of this hydrolysis. The rate of hydrolysis does not depend significantly on pH in the range of pH 4.7 to 9.2 (see Table 2):

Table 2. Effect of pH on half-life

	pH 5	pH 7	pH 9
Half-life	43 hours	69 hours	45 hours

Consideration of the triforine half-life indicates that triforine in aqueous solution is inherently unstable, which is confirmed by the test results provided by ACA and collected by the NRA.

3.1.3 Stability of triforine in products under review

Given the finding that triforine is inherently unstable in aqueous solution, the NRA investigated the relevance of this fact to the five products under review. The NRA is not able to release specific details of product formulations, as they are confidential. However, our examination of the formulations indicated that none contained chemicals capable of stabilising triforine in aqueous solution to the extent that the amount declared on the respective label would be met while the products are stored in accordance with their respective label instructions.

3.2 EFFECTIVENESS

3.2.1 Assessment of effectiveness

On the basis that it would be likely that product containing triforine in aqueous solution would contain triforine at levels below the label declared amount and also the empirical evidence from testing, the review recommended that the products, when used according to their respective label instructions, would not be likely to be effective according to the NRA's criterion that each product contain triforine at the level specified on their respective approved label(s).

4. CONCLUSIONS

The review concluded and made recommendations that it was likely that products containing triforine in aqueous solution would not contain the level of triforine stated on labels and that therefore they would not be effective fungicides. As noted, however, the registrations had already been cancelled before the review was completed.

5. DEALING WITH CANCELLED PRODUCTS

5.1 INSTRUCTIONS FOR USING OR OTHERWISE DEALING WITH CANCELLED PRODUCTS

As indicated, the NRA has cancelled the registrations of all products containing triforine in aqueous solution. The NRA has also issued instructions for using or otherwise dealing with cancelled product.

5.1.1 Possession

The NRA has determined that any person possessing stocks or batches of these cancelled products on or prior to their respective date of cancellation only where that possession is consistent with the NRA's instructions for dealing with existing stocks.

5.1.2 Supply

The NRA has determined that a person must not supply or cause to be supplied these cancelled products except for the purposes of returning product to the registrant or point of sale.

5.1.3 Use

The NRA has determined that persons already in the possession of cancelled product can continue to use the product according to its label instructions, despite its ineffectiveness as a fungicide, as to do so would pose no risk to consumers. Rather than making it an offence for consumers to use an ineffective product, products are being recalled. Where product labels have instructions for use as an insecticide, use in accordance with those instructions would afford a safe and simple method of disposing of the product.

5.2 RECALL ACTION

This report notes that these cancelled products are being recalled to clear cancelled product from supply points and to provide a mechanism for the return of purchased product, should consumers wish to do so.