

***Agrobacterium radiobacter* strain K1026 (006474) Technical Document**

Issued 9/99

I. Abstract

Agrobacterium radiobacter strain K1026 is a microbial pesticide that can be used to treat germinating seeds or roots and stems of certain stone fruit and nut trees and ornamentals to protect them from crown gall disease. Products are intended for use in the greenhouse or in nurseries. EPA has approved the use of this pesticide until fall 2001 while it waits for additional data to more fully characterize the identity of the microbe. However, based on the available information, the use of the pesticide is not expected to have any adverse effects on human health or the environment.

Agrobacterium radiobacter strain K1026, is the result of a simple genetic alteration of a naturally occurring bacterium *Agrobacterium radiobacter* strain K84. Except for the deletion of a small portion of DNA removed in K84, the two strains are essentially identical and have the same characteristics. Removal of this genetic material prevents the transfer of resistance from strain K1026 to other strains. The naturally occurring bacterium *Agrobacterium radiobacter* strain K84 is widespread in soil and found near plant roots. A toxic compound produced by both K1026 and K84 controls certain other *Agrobacterium* spp. that cause crown gall disease.

Based on review of the available toxicology and pathogenicity data and other information related to *Agrobacterium radiobacter* strain K1026, EPA finds that this microbe is not likely to produce adverse effects in humans. A very similar organism, *Agrobacterium radiobacter* strain K84, has been used for approximately twenty years without any reports of adverse effects or reactions. *Agrobacterium radiobacter* strains K1026 and K84 are not known to cause any infectious diseases in humans. This microbial pesticide is not intended for use on food crops. Consequently, it is not likely to pose a hazard to human adults, infants, children, or other sensitive subpopulations via the dietary route of exposure. The potential aggregate exposure, derived from non-dietary and non-occupational exposure, should be minimal or non-existent. EPA is requiring growth temperature variation measurements to more definitively characterize risks to human health.

The Tier 1 ecotoxicology studies were waived based on the derivation of *Agrobacterium radiobacter* strain K1026 from strain K84, minimal exposure to non-target organisms, and no evidence of any unintended effects on non-target species by strain K84. Based upon this evaluation, the EPA has determined that *Agrobacterium radiobacter* strain K1026 is likely to pose only a minimal risk to the environment or non-target organisms. EPA is requiring

substrate utilization tests with K1026 and K84 to alleviate discrepancies in previously submitted tests and confirm the lineage of K1026.

II. Overview

A. Product Overview

- **Microbial Pesticide Name:** *Agrobacterium radiobacter* strain K1026 OPP
- **Trade Name(s):** NOGALL
- **Chemical Code:** 006474

Basic Manufacturer: Bio-Care Technology Pty Limited ("Bio-Care")
RMB 1084 Pacific Highway
Somersby, NSW 2250
AUSTRALIA

US Agent: Ms. Amy Roberts
Technology Sciences Group Inc.
1101 17th Street, N.W.
Suite 500
Washington D.C. 20036-4704

B. Use Profile

- **Type of Pesticide:** Microbial control agent
- **Mechanism of action:** *Agrobacterium radiobacter* strain K1026 is a biological control agent for the prevention of crown gall disease caused by the infection of nursery stock by many virulent strains of *Agrobacterium tumefaciens* and *A. rhizogenes*. Control of crown gall disease in susceptible hosts is largely due to the production of agrocin 84 and root colonization by *Agrobacterium radiobacter* strain K1026 contained in NOGALL.
- **Use Sites:** Terrestrial and Greenhouse Non-food and Non-Bearing Crops

NOGALL is used to treat germinating seeds or roots and stems of certain non-bearing stone fruit and nut trees and ornamentals.

Applied to germinating seeds of non-bearing: almond, apricot, cherry, nectarine, peach, plum, prune, walnut, and pecan.

Applied to roots and stems of non-bearing: almond, pecan, apricot, caneberries, cherry, nectarine, peach, plum, prune, walnut, and ornamentals such as euonymus and rose.

Applied to cuttings of non-bearing: almond, pecan, apricot, caneberries, cherry, nectarine, peach, plum, prune, walnut, and ornamentals such as euonymus and rose.

- **Target Pests for Active Ingredient:** Virulent strains of *Agrobacterium tumefaciens* and *Agrobacterium rhizogenes*
- **Formulation Types Registered:**
 - **Type:** End-use product
 - **Form:** 0.25% *Agrobacterium radiobacter* strain K1026 in a concentrated, moist peat bacterial culture
- **Method and Rates of Application:**

NOGALL is applied as a dip solution (as an inoculant) to germinating seeds, roots and stems, and cuttings in nurseries and greenhouses.

The NOGALL culture of strain K1026 contains not less than 1,000 million colony forming units (cfu) per gram of moist peat medium. NOGALL is shipped as packs of 100g or 500g of concentrated, moist peat bacterial cultures. Use at the rate of 100g per gallon or 500g per 5 gallons of cool, clean, chlorine free water. When mixed as directed, it will provide a suspension of not less than 2.64×10^7 cfu per milliliter in the dip solution. A 100g or 500 g pack properly mixed in water will treat 1,000 and 5,000 bare root seedling (1/4 inch caliper), respectively.

For root and stem application: Seedlings of stone fruit trees, nut trees and roses should be treated with NOGALL within 2 hours of lifting, root pruning or other handling operations that damage plant tissue and before and after cold storage. Bare root stock should be dipped or sprayed with NOGALL solution until all root surfaces and the stem above the bud or graft union are completely wet, or spray these tissues to runoff. Replace treatment suspension after treating the equivalent of 1,000 plants/gallon of suspension or sooner when larger trees are dipped or when the suspension becomes excessively dirty. Larger plants may require 10-15 gallons of suspension per 5,000 plants.

For germinating seed application: Dip 15 pounds of seed into a suspension of NOGALL prepared by adding 100g of NOGALL to 1 gallon of clear, unchlorinated water in a clean container. Do not allow the seed to completely dry before sowing. Do not hold diluted suspension more than 8 hours.

For cuttings: Cuttings are treated by dipping clean basal ends in NOGALL suspension. Use 100g per gallon of water as described above. Treat cuttings with NOGALL before and after cold storage.

C. Regulatory History

Bio-Care submitted an application on July 22, 1997 for registration of NOGALL containing the active ingredient, *Agrobacterium radiobacter* strain K1026. *Agrobacterium radiobacter* strain K1026 is a derivative (deletion of specific genetic material) of the previously registered active ingredient *Agrobacterium radiobacter* strain K84. Removal of this genetic material prevents the transfer of resistance from strain K1026 to other strains. Strain K84 was registered in 1979 (EPA Reg. No 40230-1) for the prevention of crown gall disease in certain fruit, nut and ornamental nursery stock (non-bearing plants only). A Reregistration Eligibility Document (RED) was published in June of 1995 allowing the reregistration of strain K84. A notice of receipt of the application for registration of *Agrobacterium radiobacter* strain K1026 as a new active ingredient was published in the [Federal Register](#) (volume 63, number 80, pages 20629-20630) on April 27, 1998 with a 30-day comment period. No comments were received as a result of this publication.

III. Science Assessment

A. Physical and Chemical Properties Assessment

Product Identity and Characterization:

The Agency has classified *Agrobacterium radiobacter* strain K1026 as a microbial pesticide. NOGALL contains living *Agrobacterium radiobacter* strain K1026 as the active ingredient. The optimal growth conditions for this bacteria include a temperature of approximately 30EC and an optimum pH of 6.8-7.1.

The genus *Agrobacterium* is a member of the *Rhizobiaceae*, which includes several related genera, in particular the legume symbionts of the genera *Rhizobium* and

Bradyrhizobium. The family is known for members that interact intimately with their host plants, causing modification of host tissue. In the case of *Agrobacterium tumefaciens*, insertion of bacterial DNA into the host genome occurs. *Agrobacterium radiobacter* strain K1026 is a derivative of the previously registered active ingredient *A. radiobacter* strain K84.

The genus *Agrobacterium* consists of gram negative, non-spore forming rods with a few peritrichous flagella. No serious human pathogens are closely related to *Agrobacterium radiobacter* though some member of the species have been associated with rare nosocomial infections. The family is also unusual in that several species have been recently identified as possessing several chromosomes.

Agrobacterium radiobacter strain K1026 was derived from K84 by marker exchange mutagenesis, during which a precise region of the genome is deleted through homologous recombination (exchange of genetic material based on alignment of identical DNA sequences). During this process, the only likely change is the removal of a defined piece of DNA from the original strain. In the present case, a section of DNA containing much of the region controlling the conjugational transfer of DNA between K84 and other bacterial strains was removed. K84 has the ability to transfer, to plant pathogenic *Agrobacterium* spp., DNA conferring immunity to a K84 biocontrol factor (agrocin 84). This trait could potentially limit the usefulness of K84 in some circumstances, and has been eliminated or greatly reduced in K1026.

While submitted data suggest that the maximum growth temperature for *Agrobacterium radiobacter* strain K1026 is less than 35 E *Agrobacterium radiobacter* strain K1026. This suggests that growth might have occurred at greater than 35 E C, and possibly, 37 E C. Survival at human body temperature would raise the possible hazard to humans that K1026 might be an opportunistic pathogen. Therefore, the Agency is asking the registrant to repeat the maximum growth temperature studies.

Product chemistry data which support the registration of *Agrobacterium radiobacter* strain K1026 are summarized in Table 1. New growth temperature data have been requested to replace MRID 443473-02 and upgrade MRID 444290-02. New substrate utilization data for K1026 and K84 have been requested to upgrade MRID 447943-01.

Table 1. Physical and Chemical Properties for *Agrobacterium radiobacter* strain K1026

eline No	Study	Results	MRID No.
Product Identity and Disclosure of Ingredients	Supplemental (no upgrade required) Supplemental , upgradable	44429001 44429002	

	Acceptable	44429003
	Acceptable	44429004
	Acceptable	44429006
	Acceptable	44347301
	Unacceptable	44347302
	Acceptable	44347303
	Acceptable	44694001
	Supplemental (no upgrade required)	44694002
	Supplemental , upgradable	44794301
	Acceptable	44694003
Manufacturing Process	Acceptable	44429005
	Acceptable	44429007
	Supplemental , upgradable	44794301
Formation of Unintentional Ingredients	Acceptable	44429007
	Acceptable	44694003
	Acceptable	44429006
Analysis of Samples	Acceptable	44347306
	Acceptable	44347307
	Acceptable	44347304
	Acceptable	44429008
	Acceptable	44347305
Certification of Limits	Acceptable	44347306
	Acceptable	44347307
	Supplemental , upgradable	44794301
Product Chemistry	Acceptable	Acceptable
	Acceptable	Acceptable
	Supplemental , upgradable	Supplemental , upgradable

B. Human Risk Assessment

There are no unreasonable adverse effects that would result from exposure to Agrobacterium radiobacter strain K1026. This includes all routes of exposures for which there is reliable information.

1. Human Toxicity Assessment

a. Acute Toxicity

All mammalian toxicology data requirements have been submitted and adequately satisfy data requirements to support registration. The acute oral, acute pulmonary toxicity/pathogenicity, and acute dermal irritation studies resulted in Toxicity Category IV classifications and indicated that the microbial biological control agent is not pathogenic or infective in a single dose. The primary eye irritation test resulted in a Toxicity Category III classification based upon the dose level. In the acute intra-peritoneal

toxicity/pathogenicity study, *Agrobacterium radiobacter* strain K1026 demonstrated no signs of toxicity or infectivity.

Table 2. Toxicity Data Requirements

Line No	Study	Results	MRI ID
	Acute Oral Toxicity/ Pathogenicity	Acceptable , Toxicity Category IV (Rats); clearance not monitored	4442900
	Acute Oral Toxicity/ Pathogenicity - Limit Test	LD ₅₀ of <i>Agrobacterium radiobacter</i> strain K1026 in rats is > 1.21 X 10 ⁸ cfu/animal. Acceptable , Toxicity Category IV	4442900
	Acute Dermal Irritation	Acceptable , Toxicity Category IV	4442901
	Acute Dermal Irritation - Limit Test	The LD ₅₀ of <i>Agrobacterium radiobacter</i> strain K1026 in rats is >500 mg/animal. Acceptable , Toxicity Category IV	4442901
	Acute Pulmonary Toxicity/ Pathogenicity	Acceptable , Toxicity Category IV; clearance within four days	4442901
	Acute Pulmonary Toxicity - Limit Test	The LC ₅₀ of <i>Agrobacterium radiobacter</i> strain K1026 is > 1.8 X 10 ⁸ cfu/animal in rats. Acceptable , Toxicity Category IV	4442901
	Acute Intra-Peritoneal Toxicity/Pathogenicity	Acceptable	4442901
	Acute Eye Irritation	Acceptable , Toxicity Category III	4442901
	Hypersensitivity Incidents	Incidents of hypersensitivity must reported under FIFRA section 6(a)2 when/if they occur.	

b. Subchronic Toxicity and Chronic Toxicity

Subchronic and chronic toxicity were not required because survival, replication, infectivity, toxicity, or persistence of *Agrobacterium radiobacter* strain K1026 was not observed in the test animals treated in the acute oral or pulmonary infectivity tests.

2.

3. Effects on the Immune and Endocrine Systems

The Agency has no information to suggest that *Agrobacterium radiobacter*, strain K1026, has an effect on the immune and endocrine systems. No specific tests have been conducted with *Agrobacterium radiobacter* strain K1026, to determine such effects. However, as is expected from a non-pathogenic microorganism, the submitted toxicity/pathogenicity studies in rodents indicated that following pulmonary exposure, the immune system is still intact and able to process and clear the active ingredient. No serious human pathogens are closely related to *Agrobacterium radiobacter* though some members of the species have been associated with rare nosocomial infections. The production of the toxin, agrocin 84, is not expected to have

any estrogenic or endocrine effects on non-target organisms. The Agency is not requiring specific information on the endocrine effects of this biological pesticide at this time.

4. **Dose Response Assessment**

No toxicological endpoints are identified.

5. **Dietary Exposure and Risk Characterization**

The proposed nursery and greenhouse, non-food and non-bearing plant uses do not pose a dietary risk to humans because dietary exposure is minimal or non-existent if the pesticide is used as labeled.

6. **Occupational, Residential, School and Day Care Exposure and Risk Characterization**

Occupational Exposure and Risk Characterization

Based on the anticipated application methods for end-use products formulated from *Agrobacterium radiobacter* strain K1026, the potential for dermal, eye, and inhalation exposures for pesticide handlers exists. Because of the expected lack of significant mammalian toxicity, occupational exposure data to the active ingredient are not required at this time. However, to further mitigate potential eye exposure, the Agency is requiring Toxicity Category III labeling for eye irritation. In addition, since the active ingredient is a living microorganism, a NIOSH dusk mask labeling statement (as indicated in Section V below), is required for end-use products to further mitigate against risk due to inhalation.

Occupational exposure and subsequent risks are considered to be negligible because strains of *Agrobacterium radiobacter* have rarely been implicated in human pathogenicity and have not been reported to be pathogenic to animals. The risks are also expected to be minimal based on evaluation of submitted Tier I acute toxicity tests for *Agrobacterium radiobacter* strain K1026 (Table 2). Because of the low toxicity of *Agrobacterium radiobacter* strain K1026, the Re-Entry Interval for uses within the scope of Worker Protection Standard is 4 hours. In addition, the product labeling stipulated in the Labeling section (section V. Actions Required of Registrants) will adequately mitigate the risks to handlers.

a. **Residential, School and Day Care Exposure and Risk Characterization**

The use sites are listed as greenhouses or nurseries where the pesticide is intended to control crown gall disease on non-food and non-bearing crops. The toxicology of the active ingredient indicates that there will be minimal to nonexistent nondietary risk to children present from use sites allowed in end-use products formulated from *Agrobacterium radiobacter* strain K1026. No indoor residential, school, or day care uses currently appear on the label.

7. **Drinking Water Exposure and Risk Characterization**

Agrobacterium radiobacter strain K1026, is a simple deletion mutant of the naturally-occurring *Agrobacterium radiobacter* strain K84. *Agrobacterium radiobacter* is not known as an aquatic bacterium, and therefore, is not expected to proliferate in aquatic habitats. Although the potential exists for some minimal amount of the applied *Agrobacterium radiobacter* strain K1026 to enter ground water or other drinking water sources, the amount present, in all probability, would be undetectable or at least several order of magnitude lower than those levels tested for safety. Also, drinking water is not screened for *Agrobacterium radiobacter* strain K1026 as potential microbial contaminant or a direct pathogenic contaminant. However, the municipal treatment of drinking water would further reduce the possibility of exposure to *Agrobacterium radiobacter* strain K1026 through drinking water. Therefore, the Agency considers the potential of significant transfer of *Agrobacterium radiobacter* strain K1026 to drinking water as minimal to nonexistent.

8. **Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children**

This microbial pesticide is not intended for use on food crops. Consequently, it is not likely to pose a hazard to human adults, infants, children, or other sensitive subpopulations via the dietary route of exposure.

9. **Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation**

The health risk is expected to be negligible from the potential aggregate exposure from dermal, oral, and inhalation routes, as stated above. The potential aggregate exposure derived from dermal and inhalation exposure via mixing, loading, and applying *Agrobacterium radiobacter* strain K1026;

the dietary exposure from drinking water; and treated produce containing this organism, should fall well below the currently tested microbial safety levels. In summary, the potential aggregate exposure, derived from non-dietary and non-occupational exposure, should be minimal if non-existent.

10. Cumulative Effects

Agrobacterium radiobacter strain K1026 is practically non-toxic to mammals. No mechanism of toxicity in mammals has been identified for this organism. Therefore no cumulative effect with other related organisms is anticipated.

C. Environmental Assessment

0. Environmental Fate

At least two studies in the general scientific literature have examined the fate of *Agrobacterium radiobacter* strains K84 or K1026 in the soil and root associated regions (rhizosphere) of several plant species (Stockwell *et al.*, 1993 and Vicedo *et al.*, 1993). Vicedo and colleagues demonstrated that strains K84 and K1026 colonized peach roots to essentially the same extent. Stockwell and colleagues examined the fate of strain K84 applied to cherry roots or soil. Populations of strain K84 applied to cherry roots at a rate of between 10^6 and 10^7 cfu/g fresh weight of root fell to around 10^5 cfu/g fresh weight of root in 5 to 10 weeks time, a level comparable to those previously found for *Agrobacterium* spp. Populations of strain K84 applied to field soil at a rate of over 10^5 cfu/g dry weight of soil fell to less than 10^2 cfu/g and undetectable levels in 16 weeks. However, by using a trap crop, it was shown that strain K84 did not disappear from the soil.

Therefore, using the data of Vicedo to infer that strain K1026 would behave similarly to strain K84, it is likely that strain K1026 will fall to levels typical for naturally occurring *Agrobacterium radiobacter* strains within about 10 to 20 weeks of application. In addition, these data suggest that strain K1026 will not entirely disappear from the soil.

1. Ecological Toxicity

The Tier 1 ecotoxicology studies were waived based on the derivation of strain K1026 from strain K84, expected minimal exposure to non-target organisms based on the proposed use pattern, and lack of evidence of any undesired effects on non-target species despite long-term product use of K84

[see Letter J. Andersen to D. Bullard, April 21, 1998 communicating acceptance of the waiver request; Memorandum D. Gurian-Sherman and G. Tomimatsu to S. Matten, April 7, 1998, evaluation of the request]. Data were submitted by Bio-Care showing that K1026 is derived from K84 by a simple deletion of a small region of DNA responsible for the conjugal transfer to other *Agrobacteria* of the agrocin 84 plasmid. Furthermore, data above suggest that K84 and K1026 will behave similarly in the soil. Therefore, the Tier 1 ecotoxicology studies were waived and the risk posed by strain K1026 is expected to be minimal to non-target organisms.

The waiver request is also supported by the findings presented in the reregistration eligibility document of K84 published in June 1995. This document found that K84 is well characterized and has been in continuous use since 1979 without reported adverse incidents to non-target organisms. It was also determined that the registered uses of K84 are essentially identical to those of K1026 and these uses pose minimal exposure of non-target organisms. In addition, literature searches conducted for the current assessment of strain K1026 found no adverse impacts on non-target organisms.

However, some of the submitted substrate utilization studies did not show the same results for K1026 and K84. This means there is some uncertainty with the claimed lineage of K1026 derivation from K84. Additional substrate utilization data are requested as a condition of registration to resolve these differences and confirm the expected results. These discrepancies are listed below in the "Data Gaps" section. Therefore, the ecological toxicity data are waived pending the resolution of these phenotypic differences. Additional ecological toxicity data may be required if these discrepancies cannot be resolved.

IV. Public Interest Findings

The Agency believes the use of Bio-Care's *Agrobacterium radiobacter* strain K1026 under this registration would be in the public interest. The criteria for Agency evaluation of public interest findings is outlined in 51CFR No. 43, Wednesday March 5, 1986. Under part IV.A, the proposed product may qualify for an automatic presumptive finding if it is for minor use, is a unique replacement for pesticides of concern, or is for use against a public health pest. *Agrobacterium radiobacter* strain K1026 is intended for formulation into end-use products for control of crown gall disease. Almost of all of the uses are for minor use crops and therefore,

the product qualifies for an automatic presumptive finding and is presumed to be in the public interest. However, because not all end-uses are for minor crops, the Agency has determined that the registration of *Agrobacterium radiobacter* strain K1026 is in the public interest because of its efficacy and additional safety as compared to other registered alternatives.

First, there are no effective registered alternatives for the control of crown gall disease except for strain K84. Second, strain K1026 has been genetically modified to greatly reduce the chance of genetic exchange between K1026 and the pathogenic *Agrobacterium* spp. in soil, thus stopping any immunity buildup of the crown gall disease-causing bacteria.

The currently registered product, *Agrobacterium radiobacter* strain K84, has been found to have the capability of transferring its antibiotic and immunity genes to the pathogenic strains (strains that cause crown gall) rendering the known antibiotic strains useless for disease control. Strain K1026 was developed by modifying strain K84 so it could not transfer plasmid to other organisms. Strain K1026 has proven to be stable and to still produce the antibiotic (bacteriocin) in equal amounts to strain K84. This implies there is now a strain which will control the disease-causing strains, but not transfer genetic material to the disease causing strains. While this situation is not explicitly within the conditions for a public interest finding, K1026 provides a control which is superior to the only alternative control strain K84 since it does not transfer resistance to this strain to other strains. This means that K1026 provides certain advantageous environmental fate characteristics when compared to K84. Resistance to strain K84 would result in significant but non-quantified economic losses to specific nurseries as the resistance spread. Therefore, we find it is in the public interest to grant a conditional registration for *Agrobacterium radiobacter* strain K1026.

V. Risk Management and Registration Decision

A. Determination of Eligibility

Pursuant to FIFRA section 3(c)(7)(C), EPA may conditionally register a new pesticide active ingredient if: 1) insufficient time has elapsed since the imposition of the data requirement for those data to be developed and all other required data have been submitted, 2) the use of the pesticide product during the period of the conditional registration will not cause any unreasonable adverse effect on the environment, and 3) the registration and the use of the pesticide during the conditional registration is in the public interest. The Agency believes that all these criteria have been fulfilled.

The first criterion has been met because insufficient time has elapsed since the imposition of the data requirements described in part V. Action Required by Registrants. Agency scientists have reviewed the data submitted or cited by Bio-Care

with respect to health effects and ecological effects and have identified no significant hazards to human health or non-target organisms. However, to confirm these expected results, the additional data described in part V. will be required as conditions of registration.

The applicant has submitted or cited data to satisfy the second criterion. Bio-Care has submitted and/or cited satisfactory data pertaining to the proposed use of the product. The human health effects data and nontarget organism effects data are considered sufficient for the period of the conditional registration. These data demonstrate that no foreseeable human health hazards or ecological effects are likely to arise from the use of the product during the conditional registration. In view of these minimal risks, the Agency believes that the use of the product during the limited period of the conditional registration will not cause any unreasonable adverse effects.

Although the data with respect to this particular new active ingredient is satisfactory, it is not sufficient to support an unconditional registration under FIFRA 3(c)(5). Additional data are necessary to evaluate the risk posed by the continued use of this product. These data requirements are specified in part V. of this document.

The Agency also believes that the third criterion for a FIFRA 3(c)(7)(C) conditional registration has been fulfilled because the use of Bio-Care's *Agrobacterium radiobacter* strain K1026 under this registration would be in the public interest. The criteria for Agency evaluation of public interest findings is outlined in 51CFR No. 43, Wednesday March 5, 1986. Under part IV.A, the proposed product may qualify for an automatic presumptive finding if it is for minor use, is a unique replacement for pesticides of concern, or is for use against a public health pest. *Agrobacterium radiobacter* strain K1026 is intended for formulation into end-use products for control of crown gall disease. Almost of all of the uses are for minor use crops and therefore, the product qualifies for an automatic presumptive finding and is presumed to be in the public interest. However, because not all end-uses are for minor crops, the Agency has determined that the registration of *Agrobacterium radiobacter* strain K1026 is in the public interest because of its efficacy and additional safety as compared to other registered alternatives as described in part IV. of this document.

Therefore, *Agrobacterium radiobacter* strain K1026 is eligible for a conditional registration. The uses are listed in Section II, B. Use Profile. Food uses are not eligible for strain K1026 at this time.

B. Regulatory Position

0. **Conditional Registration**

Based on the submitted data, the Agency is requiring a conditional registration (FIFRA 3(c)(7)(C)) of products that contain *Agrobacterium radiobacter* strain K1026 as the sole active ingredient.

1. **Tolerances for Food Uses and /or exemptions**

There are no food uses pertaining to the registration of *Agrobacterium radiobacter* strain K1026, therefore, there are no tolerance issues.

2. **CODEX Harmonization**

There are no CODEX harmonization considerations since there are no food uses associated with this registration.

3. **Risk Mitigation**

Because the active ingredient is a living microorganism, a NIOSH dusk mask labeling statement (as indicated in Section V below), is required for end-use products to further mitigate against risk due to inhalation. There are no risk issues for dietary risk, occupation and residential risk, risks to non-target organisms (plants and wildlife), or ground and surface water contamination for *Agrobacterium radiobacter* strain K1026. No risk mitigation measures are required. However, the product label will bear Environmental Hazards statements to mitigate any potential risk to aquatic species and beneficial insects caused by direct application of the microorganism to water.

4. **Endangered Species Statement**

There are no expected toxic effects on non-target species based on long-term experience with the related strain K84 and its available toxicity data. Therefore, the Agency has determined that this action will have "no effect" on listed species.

C. Labeling Rational

0. **Human Health Hazard (WPS and non-WPS)**

Agrobacterium radiobacter strain K1026 products with commercial use sites are subject to the Worker Protection Standard. Because of the low toxicity of *Agrobacterium radiobacter* strain K1026, the Re-Entry Interval for uses within the scope of WPS is 4 hours.

Precautionary statements and personal protective equipment as specified below are required based on the acute toxicity categories of this organism.

1. **Environmental Hazard**

Precautionary labeling is required as indicated below.

VI.

VII. Actions Required by Registrants

A. Data Gaps

Within twelve months from the date of the registration, Bio-Care has accepted these conditions of registration for *Agrobacterium radiobacter* strain K1026.

0. Bio-Care must repeat growth temperature studies to determine the maximum growth temperature of *Agrobacterium radiobacter* strain K1026. Bio_Care must measure the growth temperature of the incubators (or growth chamber etc.) with a calibrated measuring device accurate to 0.1 to 0.2EC several times per day (at least three to four) for several days to assure the accuracy of growth temperature measurements. Two_degree temperature intervals beginning at 29EC and up to and including 37EC should be used. Bio_Care must submit an appropriate protocol for EPA review before initiating the studies. Survival at human body temperature would raise the possible hazard to humans that K1026 might be an opportunistic pathogen.

While submitted data suggest that the maximum growth temperature for *Agrobacterium radiobacter* strain K1026 is less than 35EC, we do not have information regarding the temperature variation, the equipment or protocols for controlling temperature, or how the temperature was measured.

Depending on how these experiments were performed, actual temperatures may have varied by several degrees from the reported maximum temperature for *Agrobacterium radiobacter* strain K1026. This suggests that growth might have occurred at greater than 35EC, and possibly, 37EC. Survival at human body temperature would raise the possible hazard to humans that K1026 might be an opportunistic pathogen.

1. Bio_Care must repeat the following substrate utilization studies, using both K84 and K1026, where the results differed between the two strains in previously submitted study MRID No. [44794301](#): ribose, cellobiose, melibiose, xylitol, B_gentiobiose, D_turanose, D_ and L_fucose. These data will facilitate the determination of the lineage of K1026. Pending the results of these studies, additional non-target species or environmental fate data may be required by the Agency.

B. Reports of Adverse Effects

Reports of incidents of adverse effects to humans or domestic animals, non-target organisms, or substantiated pest resistance under FIFRA Section 6(a)2 and incidents of hypersensitivity (152-16) must be reported to the Agency when/if they occur.

C. Precautionary Labeling

Agrobacterium radiobacter strain K1026 products must state the following under the heading "PRECAUTIONARY STATEMENTS."

Hazards to Humans and Domestic Animals:

Caution: Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash thoroughly with soap and water after handling.

Personal Protective Equipment: Applicators and other handlers must wear long sleeved shirts and long pants, waterproof gloves, and shoes plus socks. As a general precaution when exposed to potentially high concentrations of living microbial products such as this, all mixers/loaders and applicators must wear a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC_21C), or a NIOSH approved respirator with any N, P, R, or HE filter.

WPS labels must state the following under the heading "**User Safety Requirements**":

Remove PPE immediately after handling this product. If gloves are worn, wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."

D. Environmental Hazards Labeling

Provided the following statement is placed into the environmental hazards statement, the risk of Agrobacterium radiobacter strain K1026 is minimal to nonexistent to non-target organisms including endangered species.

0. End-Use Product Environmental Hazards Labeling

"Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of equipment washwaters."

1. Manufacturing-Use Product Environmental Hazards Labeling

"Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public water unless this product is specifically identified and addressed in an NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA."

2. Application Rate

It is the Agency's position that the labeling for the pesticide products containing *Agrobacterium radiobacter* strain K1026 as the active ingredient complies with the current pesticide labeling requirements. The Agency has not required a maximum number of applications per a season of this active ingredient.

E. Labeling

The attached label for *Agrobacterium radiobacter* strain K1026 (EPA File # 62388-R) will be updated by the registrant to conform with the labeling requirements for *Agrobacterium radiobacter* strain K1026 stated above. Some of the essential label requirements are highlighted below.

Signal word is "Caution," based on acute eye irritation (toxicity category III). The product shall contain the following information:

- Product Name
- Ingredient Statement
- Registration Number
- "Keep Out of Reach of Children"
- Signal Word (CAUTION)
- Personal Protective Equipment (PPE) Requirements
- Environmental Hazard Statement
- Directions for Use
- Agricultural Use Requirements
- Chemigation Statement
- General Instructions and Information
- Storage and Disposal Statement

Citations Considered to be part of the Data Base Supporting the Registration of *Agrobacterium radiobacter* strain K1026

MRID	Citation
44347300	Bio_Care Technology Pty. Ltd. (1997) Submission of Product Chemistry Data in Support of the Application for Registration of <i>Agrobacterium radiobacter</i> Strain K1026. Transmittal of 7 Studies.
44429000	Bio_Care Technology Pty. Ltd. (1997) Submission of Product Chemistry and Toxicity Data in Support of the Application for Registration of Nogall. Transmittal of 13 Studies.
44694000	Bio_Care Technology (1998) Submission of Product Chemistry Data in Support of the Application for Registration of NOGALL. Transmittal of 3 Studies.
44794300	Bio_Care Technology Pty. Limited (1999) Submission of Product Chemistry Data in Support of the Application for Registration of NOGALL. Transmittal of 1 Study.
44347301	Woodhead, S.; O'Leary, D. (1997) Product Characterization__Supplemental Testing of <i>Agrobacterium radiobacter</i> Strain K1026: Lab Project Number: 6766_96_0098_BC_001: 6766_96_0098_BC_000. Unpublished study prepared by Ricerca, Inc. 41 p.
44347302	Kerr, A. (1991) Report on the Growth and Survival of <i>Agrobacterium radiobacter</i> Strain K1026 at Various Temperatures. Unpublished study prepared by University of Adelaide. 9 p. {OPPTS 885.1100}
44347303	Woodhead, S. (1997) Product Characterization__Supplemental Testing of <i>Agrobacterium radiobacter</i> Strain K1026: Biovar Determination: Lab Project Number: 6766_97_0080_AC_001: 6766_97_0080_AC_000. Unpublished study prepared by Ricerca, Inc. 37 p. {OPPTS 885.1100}
44429001	Bullard, G. (1997) Product Identity and Disclosure of Ingredients: An Overview: (<i>Agrobacterium radiobacter</i> Strain K1026). Unpublished study prepared by Bio_Care Technology Pty. Ltd. 28 p.
44429002	Gammon, R. s (1995) Product Identity and Characterization for Microbial Pest Control: <i>Agrobacterium radiobacter</i> Strain K1026: Lab Project Number: 94_1. Unpublished study prepared by Presque Isle Cultures. 77 p.
44429006	Bullard, G. (1997) Inert Ingredients: (<i>Agrobacterium radiobacter</i> Strain K1026). Unpublished study prepared by Bio-Care Technology Pty. Limited. 14p.
44694002	Morell, M.; Preston, L. (1998) A DNA_Based Diagnostic Assay for <i>Agrobacterium</i> Strains K84 and K1026. Unpublished study prepared by Australian National University. 18 p.
44694001	Bartley, S. (1998) Product Supplemental Identification and Characterisation for Microbial Pest Control (NOGALL): Lab Project Number: 98_1. Unpublished study

prepared by Pacific Laboratory Medicine Services. 20 p.

- 44794301 Bullard, G. (1999) Supplemental Information and Data Relating to MRID# 44429002: (NOGALL). Unpublished study prepared by Bio_Care Technology Pty. Limited. 121 p.
- 44429005 Bullard, G. (1997) Manufacturing Process: An Overview: (*Agrobacterium radiobacter* Strain K1026). Unpublished study prepared by Bio_Care Technology Pty. Ltd. 3 p. {OPPTS 885.1200}
- 44694003 Bullard, G. (1998) Manufacturing Process: An Overview (*Agrobacterium* Strains K84 and K1026). Unpublished study prepared by Bio_Care Technology Pty. Limited. 14 p. {OPPTS 885.1100}
- 44429007 Bullard, G. (1997) Discussion of Formation of Unintentional Ingredients: (*Agrobacterium radiobacter* Strain K1026). Unpublished study prepared by Bio_Care Technology Pty. Ltd. 17 p. {OPPTS 885.1300}
- 44347306 Gammon, R. (1993) The Determination of Viable Counts and Biocharacterization of *Agrobacterium radiobacter* K1026: Lab Project Number: 1202. Unpublished study prepared by Presque Isle Cultures. 43 p.
- 44347307 Gammon, R. (1995) Recovery and Identification of *Agrobacterium radiobacter* K1026 End Product (NOGALL): Lab Project Number: 94_2. Unpublished study prepared by Presque Isle Cultures. 54 p.
- 44249008 Bullard, G. (1997) Certification of Limits Physical and Chemical Properties: (*Agrobacterium radiobacter* Strain K1026). Unpublished study prepared by Bio_Care Technology Pty. Ltd. 4 p. {OPPTS 885.1500}
- 44347304 Gammon, R. (1993) Physical and Chemical Testing of a Microbial Pest Control Agent: NOGALL: Lab Project Number: 1201. Unpublished study prepared by Presque Isle Cultures. 41 p.
- 44347305 Bio_Care Technology Pty. Ltd. (1991) *Agrobacterium radiobacter* Strain K1026 Survival in Peat at Storage Temperatures of 4 (degrees) C and 26 (degrees) C Over 12 Months: (Final Report). Unpublished study. 6 p. {OPPTS 885.1100}
- 44429009 David, R. (1991) Acute Oral Toxicity/Pathogenicity Study of *Agrobacterium radiobacter* Strain K1026 in Rats: Final Report: Lab Project Number: G_7330.221: 1602.221. Unpublished study prepared by Microbiological Associates Inc. 23 p.
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- 44429013 David, R. (1991) Acute Pathogenicity/Toxicity Screen of *Agrobacterium radiobacter* Strain K1026 in Mice: Final Report: Lab Project Number: G_7330.213: 1602.213. Unpublished study prepared by Microbiological Associates Inc. 19 p.
- 44429012 David, R. (1991) Primary Dermal Irritation Test of Nogall in Rabbits: Final Report: Lab Project Number: G_7368.242: 1602.242.002. Unpublished study prepared by

Microbiological Associates Inc. 21 p.

44429011 David, R. (1991) Primary Eye Irritation Study of Nogall in Rabbits: Final Report: Lab
Project Number: G_7368.230: 1602.230.002. Unpublished study prepared by
Microbiological Associates Inc. 29 p.