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December 20, 2013

Isagro USA, Inc.
Allyl isothiocyanate (AITC)
Petition for Inclusion on the National List as a Synthetic Substance Allowed For Use in Organic Crop Production

Lisa Brines, Ph.D
National List Manager
USDA/AMS/NOP, Standards Division
1400 Independence Ave. SW
Room 2648-So., Ag Stop 0268
Washington, DC 20250-0268

Dear Ms. Brines,

Technology Sciences Group, Inc., on behalf of Isagro USA, Inc., hereby submits a Petition for Inclusion of Allyl isothiocyanate (AITC) on the National List as a Synthetic Substance Allowed for Use in Organic Crop Production.

Enclosed you will find the following to support this petition:

1) Allyl isothiocyanate (AITC): Petition for Inclusion on the National List as a Synthetic Substance Allowed For Use in Organic Crop Production
2) Attachment A: Confidential attachment regarding AITC manufacturing process and justification for claim of confidentiality
3) Attachmnet B: Comprehensive list of published literature documents related to toxicity, efficacy, and use of AITC
4) Dominus end-use bio-pesticide product label, containing 96.3% Allyl isothiocyanate (AITC)
5) U.S. EPA Biopesticides Registration Action Document: Oil of Mustard and Allyl isothiocyanate (AITC) dated September 11, 2013

6) U.S. EPA Science Review in support of the registration of the TGAI/MP IR9804 and the end-use product, IRF 135 (Dominus), respectively containing 99.8% and 96.3% Allyl isothiocyanate (AITC), dated May 15, 2013
7) U.S. EPA Notice of Pesticide Registration for IRF135 (alternate brand name Dominus) dated September 26, 2013
8) Final Report: Characterization of Allyl isothiocyanate (AITC) of Synthetic and Natural Origin, dated February, 2013
9) National Toxicology Program Carcinogenesis Bioassay of Allyl Isothiocyanate (CAS No. 57-06-7) In F344/N Rats and B6C3F1 Mice (Gavage Study); Technical Report Series No. 234
10) U.S. EPA Vegetable and Flower Oils Summary Document Registration Review: Initial Docket, Case 8201, dated March 2010

Thank you for coordinating the review of the enclosed petition. If you have any questions regarding the enclosed documentation or if you need additional information, please contact me at (530)757-1287.

Sincerely,

Enclosures
ZPT/Isagro NOP AITC 12-20-13

Cc M. Allan, Isagro USA, Inc.
Files

Allyl Isothiocyanate (AITC):

Petition for Inclusion on the National List as a Synthetic Substance Allowed For Use in Organic Crop Production

OVERVIEW

Allyl isothiocyanate (AITC) is a naturally occurring compound found in of Oil of Mustard (from black mustard seed, Brassica Ingra L. (Family: Cruciferae / Brassicaceae), and is produced naturally when enzymes of cruciferous plants, myrosinase and glucosolinate, are combined in the presence of water. These two enzymes are kept separate within the plant cells until the plant is attacked and or crushed whereby they then combine to form the plant defense chemical AITC. In addition to its natural occurrence in mustard, AITC can be found naturally in food commodities such as cooked cabbage, kale, mustard and horseradish.

As a synthetically produced compound AITC is manufactured from allyl iodide and potassium thiocyanate. Synthetic AITC has been approved for use by EPA as a bio-fumigant for use in crop production to control soil-borne fungi, nematodes, weeds and insects.

Isagro USA, Inc. has registered both a Manufacturing Use Product (MUP), IR9804 (EPA Reg. No. 89285-1), and an end-use product (EP), IRF135 (EPA Reg. No. 8928S-2) with EPA. The Isagro USA products contain synthetic AITC at 99.8% and 96.3%, respectively. IRF135 is labeled for pre-plant soil application only, and the active ingredient (synthetic AITC) and its degradates will dissipate prior to planting. For this reason, the Agency considers this to be a non-food use and, therefore, a tolerance or exemption from the requirement of a tolerance is not required (40 CFR Part 180.1167).

In addition, AITC is listed as "Generally Regarded as Safe" (GRAS) with the FDA and is an approved food additive for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant (21 CFR 172.S15).

The search for a technically and economically feasible organic soil fumigant alternative has been in process for more than a decade in an attempt to increase production yields that meet market demand. Current alternative organic products containing furfural, dimethyl disulfide, and crab shells, all have drawbacks. These drawbacks come in the form of limited spectrum, product availability and or regulatory restrictions that limit their use. The current alternatives provide control of single pest categories (control of weed seeds, nematodes, insects or soil borne plant diseases) but not the multiple pest categories. AITC is being registered for use as a stand-alone product for control of all pest categories, and would replace the need to use multiple products to control various weeds and pests.

ITEM A

Identification of the category the substance is being petitioned for inclusion on the National List:

1) Synthetic substance allowed for use in organic crop production

ITEM B

Product Overview:

1. The substance's common name.

Allyl Isothiocyanate (AITC)

2. The manufacturer's name, address, and telephone number.

Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

3. The intended or current use of the substance such as use as a pesticide, animal feed additive, processing aid, nonagricultural ingredient, sanitizer, or disinfectant.

The substance is intended as a biofumigant, and is registered with the U.S. Environmental Protection Agency (EPA). AITC is approved for use with multiple registrants as an insect and animal repellent, feeding suppressant, insecticide, fungicide, herbicide, and nematicide. Isagro USA's registration of AITC is as a biofumigant for use in crop production to control soil-borne fungi, nematodes, weeds and insects.

The chemical is also approved by the U.S. Food and Drug Administration as a food additive for human consumption.

4. A list of the crop, livestock, or handling activities for which the substance will be used. If used for crops or livestock, the substance's rate and method of application must be described. If used for handling (including processing), the substance's mode of action must be described.

AITC is intended for use in crop production as an biofumigant for the control of soil-borne fungi, nematodes, weeds and insects . Isagro USA's end-use product with this active ingredient is applied as a pre-plant (non-food) bare ground soil treatment to reduce or control target pests. The product is applied (1) by tractor mounted shank injection at a depth of 8-15 inches, and may be followed by a tarp overlay, or with a water seal and press wheel (2) by drip injection, also covered by a tarp overlay, and (3) by deep injection to depths greater than 17 inches, with or without tarp covering. The Isagro USA end-use product IRF135 (96.3% Allyl isothiocyanate) is applied at a rate of 10-40 gallons of product per acre (equivalent to 85-340 lbs product per acre). Isagro USA has demonstrated that AITC and its degradates dissipate prior to crop seeding or seedling transplant.

5. The source of the substance and a detailed description of its manufacturing or processing procedures from the basic component(s) to the final product.

As a naturally-occurring compound Allyl isothiocyanate (AITC) is found in Oil of Mustard (from black mustard seed, Brassica Ingra L. (Family: Cruciferae / Brassicaceae), and is produced naturally when enzymes of cruciferous plants, myrosinase and glucosolinate, are combined in the presence of water. These two enzymes are kept separate within the plant cells until the plant is attacked and or crushed whereby they then combine to form the plant defense chemical AITC. In addition to its natural occurrence in mustard, AITC can be found naturally in food commodities such as cooked cabbage, kale, mustard and horseradish.

As a synthetically produced compound AITC is manufactured from allyl iodide and potassium thiocyanate. Both natural and synthetic versions of AITC have the same chemical structure (C_4H_5NS) and CAS Number (57-06-7).

Isagro, USA, Inc. has performed an analysis comparing AITC samples of synthetic and natural origin to assess their chemical-physical characteristic similarities (Rizzo, 2013). Results of this analysis are summarized as follows:

- An analytical method for determining the content of active ingredient in Allyl Isothiocyanate (AITC) technical product was developed and validated for specificity, linearity and precision, according to SANCO/3029/99 rev. 4 (11/07/2000).
- The content of active ingredient in AITC technical product was assessed by GC/FID with split/splitless injection method. Since AITC is present in equilibrium mixture with its isomer Allyl Thiocyanate (ATC), that quickly converts to the isomer by allylic rearrangement at the temperatures commonly used with the split/splitless injection system, the active ingredient content was determined as sum of AITC and ATC isomers. Then the actual ratio of the isomers was determined by 1H-NMR.
- Two AITC samples, batch#QJH1203012 of synthetic origin and batch#1050120806/11 of natural origin, were analyzed for active ingredient content and characterized by GC/MS, 1H-NMR, IR and UV/VIS spectroscopy.
- Refractive index, boiling point and density were also determined on both samples.
- The gaschromatographic purity of the samples of synthetic and natural origin is 100% and 98.93% (w/w) respectively and the AITC/ATC isomer ratio is 96/4 for both samples.
- GC/MS, 1H-NMR, IR and UV/VIS spectra of the samples (synthetic and natural origin) are comparable.
- Refractive index, boiling point and density determined in both samples are comparable.

The comparison results are summarized in table below:

	batch#QJH1203012 **synthetic origin**	batch#1050120806/11 **natural origin**
GC purity	100% (w/w)	98.93% (w/w)
NMR (AITC/ATC ratio)	96/4	96/4
GC/MS	comparable spectra	
H-NMR	comparable spectra	
IR	comparable spectra	
UV/VIS	comparable spectra	
refractive index (589 nm and 20°C)	1.531	1.532
boiling point	420 K (147°C)	422 K (149°C)
density	1.017 g/ml	1.016 g/ml

Results of the analysis indicate that AITC samples of synthetic and natural origin have comparable chemical-physical characteristics.

Isagro USA, Inc.'s manufacturing process for synthetic AITC is considered to be Confidential Business Information (CBI) and is enclosed as a confidential attachment. We have also enclosed a justification to support the CBI claim.

6. A summary of any available previous reviews by State or private certification programs or other organizations of the petitioned substance.

Not Applicable. AITC has not been reviewed by any state or private certification program.

7. Information regarding EPA, FDA, and State regulatory authority registrations, including registration numbers.

AITC is an existing ingredient with EPA (PC Code 004901), and has been granted an exemption from the requirement of a tolerance as an insecticide and repellent when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling (40 CFR Part 180.1167). The first approved use in a registered biochemical product was in 1962.

For Isagro USA, EPA has registered both a Manufacturing Use Product (MUP), IR9804 (EPA Reg. No. 89285-1), and an end-use product (EP), IRF135 (EPA Reg. No. 89285-2). The Isagro USA products contain synthetic AITC at 99.8% and 96.3%, respectively. IRF135 is labeled for pre-plant soil application only, and the active ingredient (synthetic AITC) and its degradates will dissipate prior to planting. For this reason, the Agency considers this to be a non-food use and, therefore, a tolerance or exemption from the requirement of a tolerance is not required. The EPA decision document and science reviews for Isagro USA registrations are included with this petition.

Isagro USA, Inc. is currently in the process of applying for pesticide registrations for the end use product IRF135 with state agencies, with approvals to date in the following states: GA, SC, MO, and OK.

AITC is listed as "Generally Regarded as Safe" (GRAS) with the FDA and is an approved food additive for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant (21 CFR 172.515).

8. The Chemical Abstract Service (CAS) number or other product numbers of the substance and labels of products that contains the petitioned substance.

The CAS number for AITC, for both the natural and synthetic versions, is 57-06-7. A copy of the end use label IRF135 (EPA Reg. No. 89285-2) is enclosed.

9. The substance's physical properties and chemical mode of action including (a) chemical interactions with other substances, especially substances used in organic production; (b) toxicity and environmental persistence; (c) environmental impacts from its use or manufacture; (d) effects on human health; and, (e) effects on soil organisms, crops, or livestock.

PHYSICAL/CHEMICAL PROPERTIES of IR9804 (EPA Reg. No. 89285-1), 99.8% AITC:

- Color: Colorless or pale yellow liquid
- Physical State: Liquid
- Odor: Very pungent, irritating aroma
- Stability to normal/elevated temps, metals, and metal ions: Reported stable
- Flammability: 47 °C
- pH: 4-5
- UV/visible absorption: Refractive index 1.524-1.531
- Boiling point/boiling range: 150-151°C
- Density/relative density/bulk density: 1.103-1.020
- Partition coefficient (n-octanol/water): Log P, 2.11
- Water solubility: Column elution method; shake flash: Slightly soluble in water
- Vapor pressure: 1.33 kPa @ 38.3°C

MODE OF ACTION:

a) Chemical interactions with other substances, including substances used in organic production:

AITC controls various soil borne pathogens, nematodes and weeds by acting as a general irritant and/or desiccant that may alter respiration to target diseases and pests. Following injection into the soil using a drip irrigation system or using tractor for shank application, AITC acts to reduce the population of soil borne plant diseases and pests. The soil environment left after application

is favorable for the proliferation of beneficial micro-organisms to enhance plant health and natural defenses. AITC begins to degrade in 20-60 hours post application and yields carbon, nitrogen and sulfur back to the soil. Levels of carbon act as a food source for beneficial micro-organisms much in the same way that Anaerobic Soil Disinfestation does without the need for large quantities of rice bran or mustard meal to be applied. The majority of AITC is broken down in the soil and where emissions are evident into the atmosphere at low concentrations it is rapidly broken down by ultraviolet (UV) light in less than 24hrs.

It should be noted that AITC is NOT a general soil sterilant that kills everything in the soil. Given the positive plant response following a 10 day interval from application to planting indicates that AITC creates a plant environment in the soil that is beneficial to plant growth with minimal to no negative impact on crop growth or those organisms that survive and thrive once the favorable soil environment is established post application.

AITC is chemically compatible for use with many substances currently in organic production, however, application methods must be consistent with the use instructions listed on the product labeling.

b) Toxicity and environmental persistence:

Acute and sub-chronic toxicity, developmental toxicity, and Mutagenicity of IR9804 (EPA Reg. No. 89285-1), 99.8% AITC, are discussed below in subsections c) and d).

IRF135 is an end-use product (EP) formulated from IR9804, which is a technical grade active ingredient (TGAI/MP) containing 99.8% allyl isothiocyanate (AITC). IRF135 is intended for use as a pre-plant soil treatment to control fungi, insects, nematodes and weeds. AITC is a component of many common cruciferous vegetables including broccoli and brussels sprouts, and is particularly concentrated in mustard seed, horseradish, and wasabi. Application methods via injection beneath the soil surface together with appropriate PPE will mitigate the potential for human exposure. The application methods are: (i) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, water seal or with press wheel(ii) by drip injection, also covered by tarp overlay, and 3) by deep injection to depths greater than 17 inches, with or without tarp covering. These application methods minimize the potential for exposure to non-target organisms.

AITC degrades readily in soil and water and, therefore, inhalation exposure is highly unlikely to occur after the tarps are removed following treatment (Borek et al., 1995; Pecháček et al., 1997). AITC degrades rapidly in the soil with a short half-life (T½) ranging from 20 to 60 hours (Borek et al., 1995). The average T½ of AITC in six different soil types was reported to be 47 ± 27 hours, with the greatest degradation rate of in soils that have high organic carbon and total nitrogen (N) content. In addition, the AITC T½ in soil increases with increasing moisture content and decreases in soil with increasing temperature between 10°C and 25°C. During the first 24

hours, an average of 29.8% of AITC was transformed, or degraded, and over the first 10 days at 20°C, an average of 97.1% was degraded (Borek et al., 1995). The data also demonstrate that AITC transforms in sterilized soil at the same rate as intact soil, indicating that microbial populations are not responsible for the degradation (Borek et al., 1995). The more rapid degradation that occurs in soil with higher levels of organic carbon suggests that AITC reacts with the organic material and is inactivated.

In addition, possible degradation products of AITC in soil can be proposed based on the decomposition products of AITC present in an aqueous solution in the pH range between 6 and 8, where AITC is proposed to degrade completely (Pecháček et al., 1997). Within this pH range, Pecháček et al. (1997) observed that the primary decomposition products identified at 80°C and in lower quantities at 20°C and 40°C after an 80 min incubation, were: allyl thiocyanate (ATC); allylamine (AA); and carbon disulfide (CDS). ATC, an isomer of AITC, was identified at each pH and sampling interval; AA is expected to biodegrade quickly in the environment, and so if it is formed following AITC treatment of soil, human and animal exposure is unlikely (HSDB). CDS is naturally occurring in the environment, and is released from tree roots, tidal marshes and soil (HSDB). CDS is considered ubiquitous in the environment, and so formation of carbon disulfide from treating soil with AITC would not increase exposure to non-target organisms over levels currently in the environment (HSDB, accessed 8/2012).

c) Environmental impact from use and manufacture:

AITC is a naturally occurring substance, and degrades rapidly in the soil with a short half-life (T1/2) ranging from 20-60 hours. AITC transforms in sterilized soil at the same rate as intact soil, indicating that degradation is not dependent on soil microbial populations. Products containing AITC will not be directly applied to water. However, in an aqueous solution in the pH range between 6 and 8, AITC is proposed to degrade completely. Within this pH range, the primary decomposition products identified were: allyl thiocyanate (ATC); allylamine (AA); and carbon disulfide (CDS). ATC, an isomer of AITC, was identified at each pH and sampling interval; AA is expected to biodegrade quickly in the environment, and so if it is formed following AITC treatment of soil, human and animal exposure is unlikely. CDS is naturally occurring in the environment, and is released from tree roots, tidal marshes and soil. CDS is considered ubiquitous in the environment, and so formation of carbon disulfide from treating soil with AITC would not increase exposure to non-target organisms over levels currently in the environment (EPA, 2013).

Ecological exposure and risk from AITC are expected to be minimal for non-target organisms, with the exception of honeybees. The proposed use of AITC as a pre-plant, non-food use biofumigant would mitigate exposure to honeybees as the applications are to bare soil and not to crops where honeybees would be foraging. U.S. EPA believes that Oil of Mustard and AITC will have "No Effect" on any currently listed threatened and endangered species, or any designated critical habitat, as listed by the U.S. Fish and Wildlife Service (USFWS) and the

National Oceanic and Atmospheric Administration's (NOAA) National Marine Fisheries Service (NMF5) (EPA, 2010).

Acute toxicity of IR9804 (EPA Reg. No. 89285-1), 99.8% AITC, which was submitted to U.S. EPA is outlined in the table below:

Study	Result	Toxicity Description
Avian Acute Oral	Not Required	No acute oral exposure based on application method and rapid environmental degradation
Avian Dietary	Not Required	No dietary exposure based on application method and rapid environmental degradation
Freshwater Fish LC50	96 hr LC_{50} = 0.077 ppm	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation
Freshwater Invertebrate	48-hr EC_{50} = 0.73 ppm	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation
Non-target Plants	Not Required	No non-target exposure based on application method and rapid environmental degradation
Non-Target Insects	Not Required	No non-target exposure based on application method and rapid environmental degradation

No environmental impact form the manufacture of AITC is expected. AITC is produced under good manufacturing practices.

d) Effects of human health:

Acute Toxicity of IR9804 (EPA Reg. No. 89285-1), 99.8% AITC, is outlined in the table below, along with associated U.S. EPA Toxicity Categories:

Route of Exposure	Result	U.S. EPA Toxicity Category
Acute Oral (rat)	LD_{50} = 425.4 mg/kg	II
Acute Dermal (rat)	LD_{50} = >200 mg.kg	II
Acute Inhalation (rat)	LC_{50} >0.21 mg/L	II
Primary Eye Irritation	Corrosive	I
Primary Skin Irritation	Corrosive	I
Skin Sensitization	Dermal Sensitizer	Dermal Sensitizer
Hypersensitivity	No incidents reported	N/A

Subchronic Toxicity, Developmental Toxicity, and Mutagenicity of IR9804 (EPA Reg. No. 89285-1), 99.8% AITC:

- A 90-day oral toxicity study by the National Toxicology Program (NTP, 1982) on rats dosed with 1.5-25 mg AITC/kg-body wgt/day, five days per week for 13 weeks showed No Observable Adverse Effect Level (NOAEL) of 25 mg AITC/kg-body wgt/day (the highest level tested). No mortalities occurred, and no treatment-related effects were observed on tissues obtained from the test animals when compared to non-treated controls. There were no differences in body weights between treated animals and non-treated controls.
- A 90-day dermal toxicity was not performed, based on the fact that the product is not intended for application to human skin and prolonged or repeated dermal contact is not expected when end use products for pre-plant soil treatment are applied in accordance with U.S. EPA approved use directions and PPE (for handlers: coveralls worn over long sleeve shirt and long pants, chemical resistant footwear plus socks, chemical resistant gloves, protective eyewear, and an air purifying respirator).
- A 90-day inhalation toxicity study was not performed, based on the fact that repeated inhalation exposure to AITC aerosol, vapor or gas is highly unlikely and not expected, when the end use products for pre-plant soil treatment is applied in accordance with U.S. EPA approved label use directions and PPE.
- AITC was included in a U.S. EPA study in which 16 chemically-related compounds evaluated in order to correlate potential developmental toxicity with molecular structure. In this study, no difference in the percentage of abnormal fetuses in AITC-treated offspring were detected compared to control, and no difference between treated and control in the percentage of dead fetuses was detected. The authors concluded that AITC did not display any teratogenic potential at the NOAEL of 60 mg/kg. The 60 mg/kg dose would be equivalent to 4.2 g AITC for a standard 70 kg human (EPA, 2013).
- Mutagenicity studies on AITC were conducted by the National Toxicology Program (NTP). In this battery, two reverse mutation studies confirmed that mutagenicity responses were negative in all strains tested with and without S9 activation. In three in vitro mammalian gene mutation studies, a negative response was observed in the first trial using mouse lymphoma cells without S9 activation at concentrations ranging from 0.05 to 0.8 mg/mL AITC. A second trial without S9 exhibited a significant increase in average mutant frequency and significant reduction in relative total growth at AITC concentrations of 0.4, 0.6, and 0.8 mg/mL; 1.0 mg/mL was cytotoxic. A third trial without S9 also exhibited a significant increase in average mutant frequency at concentrations of 0.6 to 1.4 mg/mL and a significant reduction in growth; a concentration of 1.6 mg/mL was cytotoxic. It is noted that the positive results were observed without S9 activation and in the presence of substantial cytotoxicity. An in vivo mammalian chromosome aberration study was conducted with mice dosed intraperitoneally with 0, 25, or 50 mg/kg AITC and compared against mice dosed with a positive control, dimethylbenzanthracine (DMBA). Increases in chromosome aberrations were not observed in AITC treated mice when compared to non-treated (negative)

controls, while a positive response was observed in DMBA treated mice. The Agency has determined that the weight of evidence demonstrates that AITC is not likely to be a mutagen. In addition, the method of application and rapid degradation rate for the proposed pre-plant soil treatment, together with appropriate PPE, mitigates exposure to humans (EPA, 2013).

U.S. EPA has considered human exposure to AITC in light of the relevant safety factors in FQPA (Food Quality Protection Act) and FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act), and determined that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of products containing AITC when label instructions are followed.

e) Effects on soil organisms, crops, or livestock:

The use of AITC as a biofumigant is intended for the control of soil-borne fungi, nematodes, weeds, and insects on a wide variety of crops. Efficacy testing using IRF135 (EPA Reg. No. 89285-2) performed by Isagro USA, Inc. over the last five years in California, Florida, and other South-Eastern states show increased yields and effective control of these organisms as compared to untreated controls in high value crops such as strawberries, tomatoes, peppers, berries, cucurbits, melons and ornamentals. The testing also indicates that IRF135 performs as well as conventional pesticides in controlling pests and increasing crop yields, and meets or exceeds the standards for crop safety (phytotoxicity).

Exposure and risk from the uses of AITC are expected to be minimal for nontarget organisms, with the exception of honey bees (EPA, 2013). The proposed use of AITC as a pre-plant, non-food use biofumigant would mitigate exposure to honeybees as the applications are to bare soil and not to crops where honeybees would be foraging. Exposure to livestock, birds, freshwater fish, freshwater invertebrates, non-target plants, and non-target insects is not expected based on the application methods proposed and the rapid environmental degradation of AITC.

EPA believes that Oil of Mustard and AITC will have "No Effect" on any currently listed threatened and endangered species, or any designated critical habitat, as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Oceanic and Atmospheric Administration's (NOAA) National Marine Fisheries Service (NMFS) (EPA, 2010).

10. Safety information about the substance including a Material Safety Data Sheet (MSDS) and a substance report from the National Institute of Environmental Health Studies.

A copy of the MSDS for the end use label IRF135 (EPA Reg. No. 89285-2) is enclosed. A substance report from the National Institute of Environmental Health Studies is not available.

11. Research information about the substance which includes comprehensive substance research reviews and research bibliographies, including reviews and bibliographies which present contrasting

positions to those presented by the petitioner in supporting the substance's inclusion on or removal from the National List.

We have enclosed a comprehensive list (Attachment B) of published literature documents related to the toxicity, efficacy, and general use of AITC. The sources for these articles include AGRICulture OnLine Access (http://agricola.nal.usda.gov/), International Agency for Research on Cancer (http://iarc.fr), and other open literature database search resources as recommended per the EPA Office of Pesticide Programs Open Literature Database Search guidance document dated July 26, 2010 (copy enclosed.

12. Petition Justification Statement for the following action requested in this petition:

2) Inclusion of a Synthetic on the National List

a) Explain why the synthetic substance is necessary for the production or handling of an organic product.

i) A single application of AITC as a pre-plant fumigant will effectively reduce the dependence on post-plant treatments, labor to support cultural practices, and will enhance market timing and yields. The use season for soil applied fumigants are nearly year round and organic AITC production is tied to seasonal availability with possible constraints from environmental impact due to negative weather conditions, thus interrupting supply timing to the marketplace.

ii) The consistency and predictability of a synthetically derived AITC insures that product volumes and timing can be matched to meet seasonal requirements for use in all target markets.

iii) Isagro USA has secured manufacturing capability at two locations to avoid any interruption of supply and with capacity that can match 1:1 the market demand.

iv) The average yield of AITC from organic production is <1% of the total tonnage per acre. Current production of AITC from organic production is available in quantities to treat less than 1,000 acres of organic production acres in the USA.

v) The cost and time to reduce organic matter and generate volumes of AITC necessary to be a viable alternative is at a cost that is significantly higher than current alternatives and prohibitive at rates necessary to deliver equivalent efficacy and yield performance. Isagro USA has secured synthetic AITC production at a price point that allows for comparable price point to current market alternatives and delivery of enhanced efficacy performance and yields while also reducing the need for some additional post plant pest and disease control practices.

vi) The target market for synthetic AITC use is targeted on more than 200K acres applied at rates of 255 – 340lbs/A. With a conservative market share estimate of 15 -30% would require approximate annual volumes between 4k – 9k MT.

a) Describe any non-synthetic substances, synthetic substances on the National List or alternative cultural methods that could be used in place of the petitioned synthetic substance.

i) The search for a technically and economically feasible organic soil fumigant alternative has been in process for more than a decade in an attempt to increase production yields that meet market demand. Organic products containing furfural, dimethyl disulfide, and crab shells, all have drawbacks. These drawbacks come in the form of limited spectrum, product availability and or regulatory restrictions that limit their use. The current alternatives provide control of single pest categories (control of weed seeds, nematodes, insects or soil borne plant diseases) but not the multiple pest categories. AITC is being registered for use as a stand-alone product for control of all pest categories. AITC is able to applied on all soil types and application methods without restriction to acres applied and a buffer zone of 0 – 25'.

ii) The use of plastic film and or mulches are effective in helping to control water retention, and temperature in the soil and the main means to enhance soil solarization. The ability of these films to provide broad spectrum control is significantly impacted due to crop rotations, seasonal and geographical impact. In order for mulches to provide solarization efficacy there must be the long term daytime temperatures to support the necessary heat units. Typically, growing regions near coastal climates do not have the capability to support ambient temperatures for mulches to be the sole efficacy solution for growers via solarization. Additionally, the length of time for solarization is extensive, typically 30 – 120 days, this time period is prohibitive as growers will plant multiple crops in a year with a short time interval between harvest and planting of the next planting. AITC is applied with the use of mulch films with many crops and the synergy between the two methods is proven as the plastic film serves as an effective barrier to enhance the exposure period of the product in a finite period of time (up to 5 days) and allows growers to have greater flexibility with planting times, environmental and market conditions.

iii) AITC is applied as a soil treatment to bare ground and as such must work as both a liquid and upon evaporation in the soil move as a gas to reach target disease and pests. Products such as hydrogen peroxide, newspaper mulches, peroxyacetic acid, soaps or composts do not have the ability to adequately distribute in the soil profile to allow contact with any consistency against target pests under conventional application methods. The formulation of AITC is optimized to allow for ease of application in irrigation water or injected with shanks in the soil where it distributes up, down and laterally all within a short time without the need for degradation prior to release of the active ingredient as in the case of mustard meal or rice bran where the organic matter must first break down to release AITC.

b) Describe the beneficial effects to the environment, human health, or farm ecosystem from use of the synthetic substance that support its use instead of the use of a non-synthetic substance or alternative cultural methods.

i) The rates applied for synthetic AITC are significantly lower compared to AITC that is a product of organic compost degradation, i.e. mustard meal or rice bran. By comparison, the proposed use rate of synthetic AITC to provide broad spectrum control against soil pests is in the range of 255 – 240 lbs/A; whereas to deliver similar AITC rates and efficacy from AITC derived organic composts a raw material rate incorporated into the soil would require 7–15MT /Acre.
   - Based on the 2011 USDA NASS reported USA acres and lbs mustard meal seed/acre the following volumes are produced before any consumption for use as an organic derived AITC soil treatment:
     - 2011 acres = 11,000
     - Yield in lbs/Acres = 490
     - If 100% of the mustard meal was used it would yield enough AITC and applied at comparable rates to synthetic rates of AITC to only treat 26 – 33 acres

ii) The excessive rate of AITC organically derived from compost has a significant problem with nitrogen that would be produced from rates at 7-15MT/acre that would deliver nitrates in the soil profile leading to groundwater contamination. Comparably the rate of synthetic AITC applied as the active release no appreciable amount of nitrogen that would influence nitrate levels in groundwater.

iii) Synthetic AITC, when applied to soil, has a predictable lifetime in the soil of less than 7 days before it breaks down and allows for planting to occur. The planting interval of 10 days insures that there are no issues to plant growth as well as workers that would enter the field to begin soil preparation are not present until well beyond it has degraded in the soil. Comparatively, the degradation curve for AITC derived from organic compost is subject organic material breakdown, AITC production, release and then subsequent degradation of the active ingredient can take up to 45+ days without restriction to workers being present in the field risking potential exposure.

Attachment B

Comprehensive list of published literature documents related to toxicity, efficacy, and use of AITC

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U.S. Environmental Protection Agency
Office of Pesticide Programs

Open Literature Database Search
Updated July 26, 2010

OPEN LITERATURE DATABASE SEARCH (*) – Updated July 26, 2010

Resource	Description	Website
AGRICOLA	AGRICultural OnLine Access	http://agricola.nal.usda.gov
ACToR	Aggregated Computational Toxicology Resource	http://actor.epa.gov/actor/faces/ACToRHome.jsp
AltBib	Bibliography on Alternatives to Animal Testing	http://toxnet.nlm.nih.gov/altbib.html
Aqualine	Comprehensive database on trade, technical and scientific literature concerning water resources	http://www.csa.com/factsheets/aqualine-set-c.php
ATSDR	Agency for Toxic Substances and Disease Registry	http://www.atsdr.cdc.gov/toxpro2.html
BIBRA Intl., Ltd.	Chemical hazard and risk assessment assitance	http://www.bibra-information.co.uk/
BIOSIS	Research database with current sources of life sciences information	http://thomsonreuters.com/products_services/science/science_products/a-z/biosis?parentKey=555184
CA DPR	California Department of Pesticide Regulation	http://www.cdpr.ca.gov/
CAWQ	Canadian Association on Water Quality	http://www.cawq.ca/en/index.shtml
CAB	Commonwealth Agricultural Bureau Abstracts	http://www.cabi.org/
CIR	Cosmetic Ingredient Review	http://www.cir-safety.org/
CSA	Life Sciences Abstracts	http://www.csa.com/news/csa-pressrelease.php
DIRLINE	Directory of Health Organizations, SIS (Specialized Information Services)	http://dirline.nlm.nih.gov/index.html
Embase	Bibliographic database in the area of biomedicine	http://library.dialog.com/bluesheets/html/bl0072.html
Enviroline	Indexing and abstracting coverage of publications reporting on all aspects of the environment	http://library.dialog.com/bluesheets/html/bl0040.html
Environmental Sciences Database	Access to scientific literature relating to all aspects of environmental quality, monitoring, resource management and conservation	http://www.ovid.com/site/catalog/DataBase/50.jsp
Health Canada	Environmental Contaminants – Reports and publications	http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php#fs
HERA	Human and Environmental Risk Assessments	http://www.heraproject.com/RiskAssessment.cfm
IARC	International Agency for Research on Cancer	http://www.iarc.fr/
ITER	International Toxicity Estimates for Risk Database	http://iter.etcnet.net/publicurl/pub_search_list.cfm
Locatorplus	US National Library of Medicine and the National Institute of Health	http://locatorplus.gov/
NCI-3D 2	National Cancer Institute Drug Information System 3D Database	http://pubs.acs.org/doi/abs/10.1021/ci00021a032

NICNAS	National Industrial Chemicals Notification and Assessment Scheme - Australia Risk Assessments	http://www.nicnas.gov.au/publications/car/default.asp
NIOSH (RTECS):	National Institute for Occupational Safety and Health (Registry of Toxic Effects of Chemical Substances)	http://www.cdc.gov/niosh/rtecs/
NLM Gateway	Resources from the National Library of Medicine	http://gateway.nlm.nih.gov/gw/Cmd
NTP	National Toxicology Program Risk Assessments	http://ntp-server.niehs.nih.gov/ntpweb/index.cfm
PBT Profiler	Persistent, Bioaccumulative, and Toxic Profiles Estimated for Organic Chemicals On-Line	http://www.pbtprofiler.net/
PubMed	US National Library of Medicine and the National Institute of Health	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi
State of NJ Health and Senior Services	Right to Know Hazardous Substance Fact Sheets	http://web.doh.state.nj.us/rtkhsfs/factsheets.aspx?lan=english&alph=&carcinogen=false&new=true
SRC/EFDB	Syracuse Research Corporation (SRC): Environmental Fate Data Base	http://www.srcinc.com/what-we-do/efdb.aspx
ToxCast™ Program	Predicting Hazard, Characterizing Toxicity Pathways, and Prioritizing the Toxicity Testing of Environmental Chemicals	http://www.epa.gov/ncct/toxcast/
Tox/Env Health subset	Environmental Health and Toxicology	http://sis.nlm.nih.gov/enviro.html
Toxnet	Toxicology Data Network: US National Library of Medicine (** all resources listed below are also available from the Toxnet homepage)	http://toxnet.nlm.nih.gov/
** **ChemIDplus**	Numerous chemical synonyms, structures, regulatory list information, and links to other databases containing information about the chemicals	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CHEM
** **HSDB**	Hazardous Substances Data Bank - Broad scope in human and animal toxicity, safety and handling, environmental fate, and more	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
** **TOXLINE**	Extensive array of references to literature on biochemical, pharmacological, physiological, and toxicological effects of drugs and other chemicals	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?TOXLINE
** **CCRIS**	Chemical Carcinogenesis Research Information System - data provided by the National Cancer Institute (NCI)	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS
** **DART/ETIC**	Developmental and Reproductive Toxicology and Environmental Teratology Information Center	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?DARTETIC

** **GENE-TOX**	Mutagenicity test data from the EPA.	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?GENETOX
** **IRIS**	Integrated Risk Information System - data from the EPA in support of human health risk assessment, focusing on hazard identification and dose-response assessment	http://www.epa.gov/ncea/iris/index.html
** **ITER**	International Toxicity Estimates for Risk – Risk information for over 600 chemicals from authoritative groups worldwide	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?iter
** **LactMed**	Drugs and Lactation Database - database of drugs to which breastfeeding mothers may be exposed. Among the data included are maternal and infant levels of drugs, possible effects on breastfed infants and on lactation, and alternate drugs to consider	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT
** **TRI**	EPA Toxics Release Inventory Program.	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?TRI
** **Haz-Map**	Occupational Exposure to Hazardous Agents	http://hazmap.nlm.nih.gov/
** **Household Products Database**	Health and Safety Information on Household Products	http://hpd.nlm.nih.gov/index.htm
** **TOXMAP**	Environmental Health e-Maps	http://toxmap.nlm.nih.gov/toxmap/main/index.jsp
** **CPDB**	Carcinogenic Potency Project	http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CPDB.htm http://potency.berkeley.edu/
ToxRefDB Program	Toxicity Reference Database	http://www.epa.gov/ncct/toxrefdb/
UK/CRD	United Kingdom/Chemicals Regulation Directorate	http://www.pesticides.gov.uk
US EPA ECOTOX	ECOTOX Database	http://cfpub.epa.gov/ecotox/quick_query.htm
US EPA HPV	High Production Volume Challenge Program	http://www.epa.gov/chemrtk/
US EPA- Pesticides	Risk Assessments	http://www.epa.gov/pesticides/
US EPA Sustainable Futures	Risk screening models used by EPA to evaluate new chemicals	http://www.epa.gov/oppt/sf/
US FDA	Food and Drug Administration - Generally Recognized as Safe (GRAS)	http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/default.htm
US FDA	Code of Federal Regulations (CFR) Title 21	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=184
WHO	World Health Organization	http://www.who.int/topics/pesticides/en/
WHO IPCS/Inchem	World Health Organization International Program on Chemical Safety, Joint Meeting on Pesticide Residues	http://www.inchem.org/pages/jmpr.html

*Disclaimer: The following websites may be helpful in conducting a literature search for your chemical. EPA cannot attest to the accuracy of information provided by these links or any other linked sites. Providing links to a non-EPA Web site does not constitute an endorsement by EPA or any of its employees of the sponsors of the site or the information or products presented on the site.

DOMINUS™

BIOPESTICIDE FOR AGRICULTURAL SOIL TREATMENT USE

A Broad Spectrum Pre-Plant Soil Biofumigant For The Control Of Certain Soil Borne Fungi, Nematodes, Weeds And Insects

ACTIVE INGREDIENT:
Allyl isothiocyanate 96.3%

OTHER INGREDIENTS: 3.7%
TOTAL: 100.0%
Contains 8.19 lbs. active ingredient (allyl isothiocyanate) per gallon. This product weighs 8.5 lbs. per gallon.

ISAGRO USA

Manufactured for:
Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

KEEP OUT OF REACH OF CHILDREN

DANGER

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, and then continue rinsing. • Call a poison control center or physician for treatment advice.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15 minutes. • Call a poison control center or doctor for treatment advice.
If swallowed	• Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything to an unconscious person. • Call a poison control center or physician for treatment advice.
If inhaled	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. • Call a poison control center or doctor for further treatment advice
NOTE TO PHYSICIAN:	
Probable mucosal damage may contraindicate the use of gastric lavage.	
HOTLINE NUMBER:	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For Chemical Emergency, Spill Leak, Fire Exposure or Accident, Call CHEMTREC Day or Night Domestic North America 800-424-9300 International 703-527-3883 (collect calls accepted).	

EPA Reg. No. 81927-4
EPA Est. No. 90105-CHN-001
Net Contents: 5 gallons (20 liters)
(Batch Code/Lot No. will be placed on the container)

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PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

DANGER. Corrosive. Causes irreversible eye damage and skin burns. May be fatal if swallowed, absorbed through skin, or inhaled. Do not get in eyes, on skin or on clothing. Do not breathe vapor. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before use.

PERSONAL PROTECTIVE EQUIPMENT (PPE)

When performing activities without the potential for liquid contact all handlers (including applicators) must wear:

- Coveralls worn over long sleeve shirt and long pants
- Chemical-resistant footwear plus socks
- Chemical-resistant (such as nitrile or butyl) gloves
- Protective eyewear
- Respirator (see below)

Where liquid contact is a potential all handlers (including mixers, loaders and applicators) in addition to the above listed PPE must wear an air purifying respirator with an organic-vapor removing cartridge with pre-filter approved for pesticides (MSHA/NIOSH approval number prefix TC-23C), or a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or a NIOSH approved respirator with an organic vapor (OV) cartridge or canister with any N, R, P or HE pre-filter.

When cleaning equipment, wear a chemical resistant apron.

Follow the manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry. Discard any clothing and or PPE that have been drenched or heavily contaminated with this product's concentrate. Do not reuse clothing or PPE that has been drenched or heavily contaminated.

ENGINEERING CONTROLS

When handlers use closed systems or enclosed cabs in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides, the handler PPE requirements may be reduced or modified as specified in the WPS at 40 CFR Part 170.

USER SAFETY RECOMMENDATIONS

- Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.
- Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

ENVIRONMENTAL HAZARDS

For terrestrial uses only. 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 when cleaning equipment or disposing of equipment wash water or rinsate.

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling. Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirement specific to your State or Tribe, consult the State/Tribal agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR Part 170. This standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. The requirements in this box apply to uses of this product that are covered by the Worker Protection Standard.

No instruction elsewhere on this labeling relieve user from complying with the requirements of the WPS.

For the entry restricted period and notification requirements, see the *Entry Restricted Period and Notification* section of this labeling. PPE for entry during the Entry Restricted Period that is permitted by this labeling is listed in the Personal Protective Equipment (PPE) section of this labeling.

Assure that labels and MSDS are on-site and readily available for employees to review.

ENTRY RESTRICTED PERIOD AND NOTIFICATION

Entry Restricted Period: Entry into the application block (including early entry that would otherwise be permitted under the WPS) by any person other than a correctly trained and PPE-equipped handler is PROHIBITED from the start of the application until 5 days after application is complete.

Notification: Notify workers of the application by warning them orally and by posting Biofumigant Treated Area signs. The sign must state:

1. "DANGER/PELIGROSO"
2. "Areas under (fumigation)(treatment). DO NOT ENTER/NO ENTRE"
3. Allyl Isothiocyanate biofumigant in use
4. Date and time of fumigation
5. Date and time entry restricted period is over
6. DOMINUS and (*name of co-application*)
7. Name, address and telephone of applicator in charge

Post the Biofumigant Treated Area sign instead of the WPS sign for this application, but follow all WPS requirements pertaining to location, legibility, text size and sign size (40 CFR § 170.120).

Post Biofumigant Treated Area signs defining the fumigation buffer zone, at all entrances to the application block no sooner than 24 hours prior to application and remain in place until at least 24 hours from the start of the application; Signs placed at the corners or on the edges of the treated area must remain posted for at least 5 days (120 hours) from the start of the application, e.g. for no less than the duration of the entry restricted period.

TERMS USED IN THIS LABELING

Application Block: The area within the perimeter of the fumigated portion of a field (including furrows, irrigation ditches, and roadways). The perimeter of the application block is the border that connects the outermost edges of the total area treated with the biofumigant product.

Start of the Application: The time at which the biofumigant is first delivered/dispensed into the soil in the application block.

Application is Complete: The time at which the biofumigant has stopped being delivered/dispensed into the soil and the soil has been sealed; drip lines have been purged (if applicable).

Entry Restricted Period: This period begins at the start of the application and expires depending on the application method and if tarps are used when the tarps are perforated and removed. Entry into the application block during this period is only allowed for appropriately PPE-equipped handlers performing handling tasks. See the *Entry Restricted Period* and *Notification* sections of this label for additional information.

Buffer Zone: An area established around the perimeter of each application block. The buffer zone must extend outward from the edge of the application block perimeter equally in all directions.

Buffer Zone Period: Begins at the start of the application and lasts for a minimum of 24-hours after the application is complete. Non-handlers must be excluded from the buffer zone during the buffer zone period.

Roadway: The portion of a street or highway improved, designed or ordinarily used for vehicular travel, exclusive of the sidewalk or shoulder even if such a sidewalk or shoulder is used by persons riding bicycles. In the event that a highway includes two or more seperated roadways, the term *roadway* shall refer to any such roadway separately.

PRODUCT INFORMATION
Apply DOMINUS as a preplant soil treatment only and as a part of an integrated pest management (IPM) program to aid in reducing or controlling the damaging effects of soil borne pests and diseases.

USE PRECAUTION
The product must only be used in a well-ventilated area. Do not use DOMINUS if it cannot be applied according to the use patterns on the label.

APPLICATION WITH OTHER PRODUCTS
DOMINUS may be applied with other pesticides or fertilizers by co-injection or co-application via the application methods outlined in this label. Consult specific product labels for additional information or restrictions concerning mix partner compatibility. Treat a small area first to ensure compatibility. Observe the most restrictive of the labeling limitations and precautions of all products used in mixtures.

SOIL TREATMENT APPLICATION METHODS
Apply as a preplant shank injection, broadcast/flat fume application, or raised bed application either shank injected into the row or in a raised bed or non-bedded strip injected through the drip irrigation system. Specific directions for each application method are provided below. Always follow label instructions to achieve optimum performance.

TARP REMOVAL, PERFORATION AND PLANTING INTERVAL
- Leave the soil undisturbed for at least 5 days after application is complete and prior to tarp cutting or perforation.
- For tarped applications, complete the cutting of the tarp or perforation/hole-punching 2 to 24 hours prior to tarp removal or planting to assist in DOMINUS dissipation.
- Tarp cutters and removers shall wear long-sleeved shirt, long pants and gloves when removing tarps following application prior to planting.
- Cold, wet, or cold and wet soils can decrease dissipation of DOMINUS and can require a longer soil exposure period.
- After application is complete, wait 10 days prior to planting.
- In addition to the 10 day waiting period, use of a Jar Seedling and/or Transplant tests for safety steps can be performed prior to planting the target crop. See page(s) 8-9 of this label for instructions.

SOIL TREATMENT TIMING AND APPLICATION RATES
- **Number of applications per year:** DOMINUS may be applied to soil as a pre-plant soil treatment prior to planting with subsequent applications allowable to the same soil within the same year provided the previous crop is completely harvested prior to application.
- **Open field:** Use 10 - 40 gallons of DOMINUS per one acre (85 - 340 lb/A).

- **Greenhouse:** Use 10 - 40 gallons of DOMINUS per one acre (85 - 340 lb/A) or 0.23 gal / 1,000ft^2 – 0.92 gal/1,000ft^2.

TABLE 1. PRE-PLANT SOIL APPLICATION RATES

TREATMENT SITE	BROADCAST EQUIVALENT RATES GAL/A*	BROADCAST EQUIVALENT RATES (LBS PRODUCT/A
Field soils to be planted to: Asparagus, brassica vegetables (broccoli, cauliflower), cereal grains, herbs and spices, leek, leafy vegetables (lettuce), legume vegetables, pineapples, root and tuber vegetables (carrot, garlic, onion, potato, sweet potato)	10 - 40	85 - 340
Field soils to be planted to: Strawberries, berries (cane fruit) , cucurbit crops (cucumber, squash, melons), fruiting vegetables (e.g. eggplant, peppers, tomatoes),	25 - 40	213 - 340
Field soils to be planted to: Fruit and nut crops, citrus, pome fruit trees, stone fruit trees, tree nuts, tropical and subtropical fruits, vineyards	30 - 40	255 - 340
Nursery, Turf, and Ornamental Soils to be planted to: Turf, lawns, parks, golf greens, athletic fields, recreational turf area, ornamentals, floral crops, forest tree seedlings	10 - 40	85 - 340
Greenhouse soils to be planted to: Food and Non-food crops	10 - 40	85 - 340
Seed or Transplant beds to be planted to:, Food crops and non-food crops	10 - 40	85 - 340
*Use the higher labeled rates for muck and heavy clay soils, as well as for those pests and or diseases such as cyst forming nematodes, *Macrophomina, Fusarium or Phytophthora* or hard coated weed seeds for example Malva, Clover or Nutsedge		

APPLICATION SITE CONDITION DIRECTIONS

Soil temperature: maximum of 90°F at a typical application depth

Soil preparation:

- Ensure the soil is well prepared and generally free at the surface of large clods. Large clods can prevent efficient soil sealing and reduce effectiveness of the product.
- Cultivate the soil to a minimum depth of 5-8" and/or equal to the desired treatment depth.
- Thoroughly incorporate plant residues into the soil to allow decomposition prior to treatment. Leave little or no plant residue present on the soil surface. Undecomposed plant material can harbor pests that will not be controlled and can interfere with the soil seal after application. Let crop residue that is present lie flat to permit the soil to be sealed effectively.
- Where applicable, fracture compacted soil layers (plow pans) within the desired treatment zone before or during application of DOMINUS.

Soil moisture:

- It is critical to maintain adequate soil moisture before, during and 48 hours post-treatment. Plan soil treatment for seasons, crop rotations, or irrigation schedules which leave adequate moisture in the soil.
- The soil must be moist (typically with enough moisture to allow weed seeds to become imbibed) from 1.5 inches below the soil surface to at least the minimum desired depth of the target treatment zone. The amount of moisture needed (typically greater than 50% Available Water Content at 9 inches) in this zone will vary according to soil type. Use the USDA Feel and Appearance Method (http://www.oneplan.org/Water/soilmoist.pdf) or a device that will accurately measure soil moisture. The surface soil generally dries very rapidly and is not considered in this determination.

Weather Conditions:

- Prior to soil treatment the weather forecast for the day of application and the 48-hour period following the soil treatment must be checked to determine if unfavorable weather conditions exist or are predicted (such as no wind speed or the potential for inversion layers) and whether soil treatment can begin.
- If significant rainfall occurs within 24 hours after DOMINUS application (enough to saturate soil that has been treated with DOMINUS), a reduction in pest control can occur.
- Apply DOMINUS in the presence of wind speeds of at least 2 mph at the start of the applications or projected to reach at least 5 mph during the application.
- Check weather forecasts 48 hours prior to application to ensure proper conditions are present at the time of application. Weather conditions and or advisories can be downloaded online at http://www.nws.noaa.gov.

Buffer Zones: Do not apply DOMINUS within 25' of any occupied structure, such as a school, daycare, hospital, retirement home, business or residence.

PRE-PLANTING AFTER APPLICATION OF DOMINUS

Recontamination Prevention:

- DOMINUS will control pests that are present in the soil treatment zone at the time of soil treatment. It will not control pests that are introduced into the soil after soil treatment

period has ended. To avoid re-infestation of treated soil, DO NOT use irrigation water, transplants, seed pieces, or equipment that could carry soil-borne pests from infested land. Avoid contamination from moving infested soil onto treated beds through cultivation, movement of soil from outside the treated zone, dumping contaminated soil in treated fields and soil contamination from equipment or crop remains. Clean equipment carefully before entering treated fields.

Testing of Treated Soils Prior to Planting:

- Allow DOMINUS to dissipate completely before planting the crop.
- When determining the appropriate time interval before planting, consideration of factors that impact DOMINUS dissipation include rate of application, depth of injection, soil temperature, soil preparation and type, soil moisture and use of various plastic films and or water sealing.
- Use of a lettuce seed and or tomato/pepper transplant test can be used to determine if sufficient time has elapsed between soil treatment and planting as described below.

Lettuce Seed Test

- After a minimum of 7 days after application proceed with the following Seed Jar test.
- Use a trowel to dig into the treated soil to a depth at or just beneath the depth of DOMINUS injection and remove 2 to 5 samples with enough soil to fill a quart sized jar half-way, mix lightly, apply moisture enough to germinate seeds, sprinkle seeds evenly over the soil surface and seal immediately with a lid for air tight conditions.
- Sample the field in several areas, especially those areas that are not representative of the general field conditions and or having higher moisture content, different soil texture or areas where rate delivery is different.
- Prepare another similar sample of untreated soil for comparison.
- Keep the jars out of direct sunlight and at a temperature of 65° to 85°F. (Direct sunlight can overheat and kill the seedlings). Lettuce seed will not germinate in the dark so place in diffuse sunlight.
- After 1 to 3 days, check each jar for seed germination.
- If seeds in the treated jar germinate and grow similar to the untreated soil sample then the treated area is safe for planting.

Tomato/Pepper Transplant Test

- After a minimum of 7 days after application proceed with the following transplant test.
- Transplant 5 to 10 healthy, actively growing tomato or pepper seedlings into treated beds at normal planting depth and several locations within the treated area. If available repeat in an area of field *not treated* with DOMINUS for comparison. If a wetter, heavier area of the treated field is available place the transplants there.
- Inspect the transplants in 3 days for plant injury including wilt, chlorosis, or leaf and root tip burn. Ensure that proper soil moisture conditions exist for transplants to remain free from water stress. If plants in the treated area are asymptomatic and or are similar in growth and appearance to plants in the non-treated area it is safe to plant.

DOMINUS DRIP (TRICKLE) CHEMIGATION APPLICATION USE DIRECTIONS:

Drip (Trickle) Chemigation Use Precautions:

- The following applies to drip (trickle) irrigation systems.
- Crop injury and a reduction in efficacy can result from non-uniform distribution of DOMINUS in irrigation water used to treat soil.

- For questions related to equipment calibration, consult your local State Extension Service specialist, equipment manufacturer or dealer.

Soil preparation:

- Ensure compacted soil layers (plow pans) within the desired treatment zone are tilled and/or fractured if it is considered normal practice before application of DOMINUS to ensure adequate soil drainage. Note that conditions where soil layers (plowpans) exist and are not tilled can result in reduced pest control, differences in planting interval or plant growth as a result of compacted or shallow soil conditions.
- The application site must be in seedbed condition. Ensure beds are listed, shaped and ready for planting.
- Ensure initial soil moisture is at ~50% of field capacity at 2 to 3 inches and down to 9 inches depth at the time of DOMINUS application. Soil texture and amount of water to be applied will impact the desired initial % field capacity necessary for drip injection.

DOMINUS Dosage:

- Determining DOMINUS dosage is based on consideration of the intended crop to be planted, treated area conditions, preparation, application method, target pest, and soil type.
- Use drip emitters with spacing of 4 to 12 inches with shallow subsurface placement to ensure thorough wetting of the soil area being treated by DOMINUS drip injection.
- DOMINUS must be metered at a target concentration between 1000 – 3000 ppm (calculated by: total volume of product to be applied / total amount of water to be applied x 1,000,000) into the water supply line and passed through a mixing device such as a centrifugal pump with by-pass agitation or static mixer to assure proper agitation and mixing to a target concentration (ppm) for even distribution before distribution into the drip irrigation system. The concentration of DOMINUS should not exceed 3000 ppm at any time during the injection period within the drip line.
- The volume of irrigation water to deliver to the treated area is dependent upon the soil type, % soil moisture or the % of field capacity at the start of the application and the target moisture level following application and equipment rising.
- Determine the irrigation water flow and adjust the flow rate of DOMINUS to meet the target ppm in irrigation water. Insert a static mixer or similar device immediately after the DOMINUS injection point to insure adequate mixing with the irrigation water.

Chemigation Application Information:

1. Apply this product only through drip (trickle) irrigation systems. Do not apply this product through any other type of irrigation system.
2. Crop injury or lack of effectiveness can result from non-uniform distribution of treated water.
3. If you have questions about calibration, contact State Extension Service specialists, equipment manufacturers or other experts.
4. Do not connect an irrigation system (including greenhouse systems) used for pesticide application to a public water system unless the pesticide label-prescribed safety devices for public water systems are in place.
5. A person knowledgeable of the chemigation system and responsible for its operation or under the supervision of the responsible person, shall shut the system down and make necessary adjustments should the need arise.

Chemigation Systems Connected to Public Water Systems:

1. Public water system means a system for the provision to the public of piped water for

human consumption if such system has at least 15 service connections or regularly serves an average of at least 25 individuals daily at least 60 days out of the year.

2. Chemigation systems connected to public water systems must contain a functional, reduced-pressure zone, back flow preventer (RPZ) or the functional equivalent in the water supply line upstream from the point of pesticide introduction. As an option to the RPZ, the water from the public water system should be discharged into a reservoir tank prior to pesticide introduction. There shall be a complete physical break (air gap) between the flow outlet end of the fill pipe and the top or overflow rim of the reservoir tank of at least twice the inside diameter of the fill pipe.

Equipment Considerations for Drip (Trickle) Chemigation Systems:

1. The irrigation system (main line, headers, and drip tape) must be thoroughly inspected for leaks before the application starts. The leak detection process requires that the irrigations system be at full operating pressure. The time required at full operating pressure will vary according to the system design and layout, soil type and target ppm concentration. Signs of leaks may include puddling along major pipes and at the top or ends of rows and/or on the bed surface or movement or shifting of beds due to bed collapse in over saturated conditions. Any leaks discovered must be repaired prior to application of DOMINUS. For leaks discovered during application of DOMINUS, immediately stop injection, wear all appropriate PPE and repair the line insuring that the problem is corrected before commencing with the drip applied injection.
2. The system must contain a functional check valve (back flow prevention device), vacuum relief valve, and low pressure drain appropriately located on the irrigation pipeline to prevent water source contamination from back flow.
3. The pesticide injection pipeline must contain a functional, automatic, quick-closing check valve to prevent the flow of fluid back toward the injection pump.
4. With use of injection pumps (e.g. Diaphragm or Centrifugal type pumps) the pesticide injection pipeline must also contain a functional, normally closed, solenoid-operated valve located on the intake side of the injection pump and connected to the system interlock to prevent fluid from being withdrawn from the supply tank when the irrigation system is either automatically or manually shut down.
5. The system must contain functional interlocking controls to automatically shut off the pesticide injection pump when the water pump motor stops or in cases where there is no water pump, when the water pressure decreases to the point where pesticide distribution is adversely affected.
6. The irrigation line or water pump must include a functional pressure switch which will stop the water pump motor when the water pressure decreases to the point where pesticide distribution is adversely affected.
7. To inject DOMINUS, use a metering device (such as a positive pressure system, positive displacement injection pump, diaphragm pump, or a Venturi system) effectively designed and constructed of materials that are compatible with pesticides and capable of being fitted with a system interlock.
8. Use of an inert gas such as nitrogen or dry compressed air is acceptable for use in a positive pressure system.

Injection System Flush After DOMINUS Application:

- **After DOMINUS injection, continue drip irrigation with clean water to flush remaining DOMINUS completely out of the system.** Apply 3 times the volume of water equivalent to the capacity of the drip injection system from the point of injection to the ends of the drip tape to ensure DOMINUS is completely voided from the injection lines and drip tape.

- Do not allow any DOMINUS to remain in the system after application.
- If common lines are used for both the DOMINUS application and to apply the water seal (if applied), the lines must be adequately flushed before starting the water seal and/or normal irrigation practices.

Soil Sealing or Tarp Use:

- When tarps are used with drip injection application, they must be in place prior to injection of DOMINUS.
- Tarp edges must be buried along the row furrow and at the ends of each row.

***Untarped* Drip (Trickle) Chemigation Applications:**

- Tarps must be used unless the drip tape is buried a minimum of 5 inches below the soil/air interface.

Planting Interval for Raised Bed Drip Applications:

- After application, leave the soil undisturbed for at least 10 days after the application is complete. Planting of the target crop is allowed at a minimum of 10 days following the completion of the application.
- Extremely cold, wet, or cold and wet soils can decrease dissipation of DOMINUS and can require a longer soil exposure and/or aeration period.
- For tarped applications, where tarp perforation or hole punching occurs allow 2 to 24 hours aeration prior to planting to assist in DOMINUS dissipation.
- Use of a Jar Seedling and/or Transplant test for crop safety can be performed prior to planting the target crop. See pages 8-9 of this label for instructions.

Requirements for Greenhouse Soil Treatment

- Applications methods for use in greenhouse soil treatment may be applied as drip injection or tractor mounted shank where applicable according to the methods described for open field with exceptions listed below:
    - All applications must be tarped or double water sealed (delivered via overhead sprinkler). Double water sealed is defined as twice the amount of water to deliver the soil treatment without causing over saturation of the soil or delivering enough water to maintain up to 80% soil moisture for 24 hours following application.
    - During the application, keep doors, vents and windows to the outside open and keep fans or other mechanical ventilation systems running within the application area.
    - Areas by which gases could enter adjacent enclosed areas must be sealed prior to application and remain closed for up to 48 hours post application.

DOMINUS TRACTOR MOUNTED SHANK RAISED BED AND BROADCAST/FLAT FUME APPLICATION USE DIRECTIONS:

Soil moisture:

- For tractor mounted shank applied treatments of DOMINUS do not apply to dry soils. Target a soil moisture reading of ~50% or greater Available Water Content to a depth of 8 to 9 inches present for at least 24 to 48 hours prior to and until the start of the application.

Soil temperature at application:

- Maximum of 90°F at application depth.

Application Methods and Equipment:

- Apply DOMINUS using chisels spaced no more than 12 inches apart and no more than 3 outlets evenly spaced per chisel (rear and forward facing type shank). The top most outlets must be no less than 5 inches from the final air soil interface.
- For shank applications the use of tarps or a water cap does not eliminate the need to remove chisel traces. Use of a press board, ring roller or other device to effectively close chisel traces must be performed.

Application Depth:

- The point of injection must be a minimum of 5 inches from the final soil/air interface. The point of deep injection must be at a minimum of 18 inches from the final soil/air interface. Use deeper placement when fumigating soil to be planted to deep-rooted plants, such as perennial fruit and nut crops, or to control deeply distributed pests.

Application Type	Injection depth	Single Sweep Chisel Spacing	Noble Plow Injector Outlet Spacing	Yetter Rig Injector Spacing	Tarped Type Sealing, Applied immediately after application*	Non-Tarped Type Sealing
Broadcast Shallow Shank	5 – 15 inches	6 – 12 inches Use of no more than 3 nozzles per sweep with 4-5 inches / nozzle and bottom nozzle at no more than 15 inches from soil surface	6 – 12 inches	4 – 6 inches	PE, VIF, TIF	Overhead sprinkler, water cap and/or Roller/Packer to compact soil surface, and close chisel traces
Broadcast Deep Shank	> 17 inches	18 – 24inches	NA	NA	NA	Roller/packer to compact soil surface
Raised bed shallow shank or Strip Application	8 – 15 inches	6 – 12 inches Use of no more than 3 nozzles per sweep with 4 – 5 inches / nozzle and bottom nozzle at no more than 15 inches from soil surface	NA	4 – 6 inches	PE, VIF, TIF	Overhead Sprinkler, water cap and/or Roller/Packer to compact soil surface, and close chisel traces

* PE = Polyethylene film; VIF = Virtually Impermeable Film; TIF = Totally Impermeable Film

Prevention of End Row Spillage:

- Do not apply or allow DOMINUS to spill onto the soil surface. Each injection line either needs a check valve located as close as possible to the soil injection point to avoid dripping or spillage. If a check valve system is not in place purge and drain the injection line prior to lifting the injection shanks from the ground.
- Only lift the injection shanks from the ground when the shut-off valve has been closed, and the DOMINUS injection line has been depressurized to passively drain remaining DOMINUS or when the system has been actively purged (e.g. via air compressor).

Injection Rig Calibration, Set-up, Repair, and Maintenance:

- DOMINUS application equipment must be calibrated and all control systems working properly. Proper calibration is critical to ensure DOMINUS application rate and soil placement. Refer to the equipment manufacturer's instructions to properly calibrate the injection equipment. The equipment dealer, local Cooperative Extension Service, crop advisor or DOMINUS dealer can provide assistance.
- Flush all equipment with water after each day's use; disassemble valves and clean carefully. All rinsate should be properly applied to the field.

Planting Interval for Raised Bed Shank and Broadcast/Flat Fume Application

- After application, leave the soil undisturbed for at least 5 days after application prior to tarp cutting or perforation/hole punching.
- For tarped applications, complete cutting of the tarp for removal or perforation/hole punching 2 to 24 hours prior to tarp removal or planting to assist in DOMINUS dissipation.
- Tarp cutters and removers shall wear long-sleeved shirt, long pants and gloves when there is no waiting or aeration period between tarp cutting and removing the tarp following application and prior to planting.
- Soil can be planted with the target crop at a minimum of 10 days following application.
- Cold, wet, or cold and wet soils can decrease dissipation of DOMINUS and can require a longer soil exposure and or aeration period.
- Soil applied under untarped shanked applications must remain undisturbed for a minimum of 10 days following completion of the application before tillage and or planting of the target crop.
- Use of a Jar Seedling and/or Transplant test for crop safety can be performed prior to planting the target crop. See pages 8-9 of this label for instructions.

PESTS CONTROLLED FROM SOIL TREATMENT USES

Nematodes

Common Name (if applicable)	Scientific Name
Ring nematode	*Mesocriconema* (=*Criconemoides*, =*Criconemella*)
Root knot nematode	*Meloidogyne*
Root-lesion nematode	*Pratylenchus*
Sting nematode	*Belonolaimus*
Stem and bulb nematode	*Tylenchus*

PESTS CONTROLLED FROM SOIL TREATMENT USES (continued)

Soil Borne Fungi

Common Name (if applicable)	Scientific Name
Charcoal rot	*Macrophomina phaseolina*
Fusarium wilt	*Fusarium spp.*
Phytophthora	*Phytophthora spp.*
Pythium	*Pythium spp.*
Rhizoctonia	*Rhizoctonia spp.*
Southern blight	*Sclerotium rolfsii*
Verticillium wilt	*Verticillium dahliae*

Insects in the Soil at the Time of Treatment

Common Name (if applicable)	Scientific Name (if applicable)
Symphylan (centipedes)	
Wireworms	

Weeds

Common Name (if applicable)	Scientific Name
California burclover	*Medicago lupulina*
Common chickweed	*Stellaria media*
Common mallow	*Malva neglecta*
Common purslane	*Portulaca oleracea*
Grasses	
Morningglory spp.	*Ipomoea spp.*
Yellow nutsedge	*Cyperus esculentus*

Mollusks: Slugs and Snails.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage and disposal.

PESTICIDE STORAGE
Store in original container in a cool, dry place.

PESTICIDE DISPOSAL
Waste resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

CONTAINER DISPOSAL for non-refillable containers
This is a non-refillable container. Do not reuse or refill this container. Empty the package completely and triple rinse container (or equivalent pressure rinse) promptly after emptying with water to be used for application. Then dispose of the empty container according to state and local regulations. Place in trash or offer for recycling if available or return it to the Seller, or, if allowed by state and local authorities, by burning. If burned stay out of smoke.

TRIPLE RINSING INSTRUCTIONS:
For rigid, nonrefillable containers small enough to shake (with capacities equal to or less than 5 gallons):

STORAGE AND DISPOSAL (continued)

Triple rinse as follows: Empty the remaining contents into application equipment or a mix tank and drain for 10 seconds after the flow begins to drip. Fill the container one-fourth full with water and recap. Shake for 10 seconds. Pour rinsate into application equipment or a mix tank or store rinsate for later use or disposal. Drain for 10 seconds after the flow begins to drip. Repeat this procedure two more times.

For rigid, non-refillable containers that are too large to shake (with capacities greater than 5 gallons):
Triple rinse as follows: Empty the remaining contents into application equipment or a mix tank. Fill the container one-fourth full with water. Replace and tighten closures. Tip container on its side and roll it back and forth, ensuring at least one complete revolution, for 30 seconds. Stand the container on its end and tip it back and forth several times. Turn the container over onto its other end and tip it back and forth several times. Empty the rinsate into application equipment or a mix tank or store rinsate for later use or disposal. Repeat this procedure two more times.

PRESSURE RINSE PROCEDURE (all sizes):
Pressure rinse as follows: Empty the remaining contents into application equipment or a tank mix and continue to drain for 10 seconds after the flow begins to drip. Hold container upside down over application equipment or mix tank or collect rinsate for later use or disposal. Insert pressure rinsing nozzle in the side of the container, and rinse at about 40 PSI for at least 30 seconds. Drain for 10 seconds after the flow begins to drip.

CONTAINER DISPOSAL for rigid, refillable containers
Refillable container. Refill this container with DOMINUS pesticide only. Do not reuse this container for any other purpose. Cleaning the container before final disposal is the responsibility of the person disposing of the container. Cleaning before refilling is the responsibility of the refiller. To clean the container before final disposal, empty the remaining contents from this container into application equipment or mix tank. Fill the container about 10 percent full with water. Agitate vigorously or recirculate water with the pump for 2 minutes. Pour or pump rinsate into application equipment or rinsate collection system. Repeat this rinsing procedure two more times.

LIMITATION OF WARRANTY AND LIABILITY
Read the entire label before using this product, including this Limitation of Warranty and Liability.

If the terms are not acceptable, return the product at once unopened for a refund of the purchase price.

This Company warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes set forth in the Directions for Use, subject to the inherent risks described below, when used in accordance with the Directions for Use under normal conditions. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, ISAGRO MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY OR ANY OTHER EXPRESS OR IMPLIED WARRANTY.

Buyers and Users of this product must be aware that there are inherent unintended risks associated to the use of this product, independent from the control of Isagro. These risks

include, but are not limited to, weather conditions, soil factors, moisture conditions, diseases, irrigation practices, condition of the crop at the time of application, materials which are present in the tank mix with this product or prior to the application of it, cultural practices or the manner of use or application, all risks which are impossible to eliminate. The Buyers and Users should be aware that these factors may cause: ineffectiveness of the product, reduction of harvested yield of the crop (entirely or partially), crop injury or injury to non-target crops or plants or to rotational crops caused by carryover in the soil, resistance of the target weeds to this product. Therefore additional care, treatment and expense are required to take the crop to harvest.

If the Buyer does not agree with the acceptance of these risks, then THE PRODUCT SHOULD NOT BE APPLIED. To the extent consistent with applicable law, by applying this product the Buyer acknowledges and accepts these inherent unintended risks and AGREES THAT ALL SUCH RISKS ASSOCIATED WITH THE APPLICATION AND USE ARE ASSUMED BY THE BUYER.

To the extent consistent with applicable law, ISAGRO or Seller shall not be liable for any incidental, consequential or special damages resulting from the use or handling of this product (including claims based in contract, negligence, strict liability, and other tort or otherwise). To the extent consistent with applicable law, the exclusive remedy of the User or Buyer and the exclusive Liability of Isagro or Seller shall be the return of the purchase price of the product, or at the election of Isagro or Seller, the replacement of the product.

To the extent consistent with applicable law, this Company does not warrant any product reformulated or repackaged from this product except in accordance with this Company's stewardship requirements and with express written permission from this Company.

Isagro or its Seller must have prompt notice of any claim so that an immediate inspection of Buyer's or User's can be made. To the extent consistent with applicable law, if Buyer and User do not notify Isagro or Seller of any claims, in proper time, it shall be barred from obtaining any remedy.

To the extent consistent with applicable law, Buyers and Users are deemed to have accepted the terms of this Limitation of Warranty and Liability, which may not be modified by any verbal or written agreement.

DOMINUS™

BIOPESTICIDE FOR AGRICULTURAL SOIL TREATMENT USE

A Broad Spectrum Pre-Plant Soil Biofumigant For The Control Of
Certain Soil Borne Fungi, Nematodes, Weeds And Insects

ACTIVE INGREDIENT:
Allyl isothiocyanate 96.3%

OTHER INGREDIENTS: 3.7%
TOTAL: 100.0%
Contains 8.19 lbs. active ingredient (allyl isothiocyanate) per gallon. This product weighs 8.5 lbs. per gallon.

ISAGRO USA

Manufactured for:
Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

KEEP OUT OF REACH OF CHILDREN

DANGER

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, and then continue rinsing. • Call a poison control center or physician for treatment advice.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15 minutes. • Call a poison control center or doctor for treatment advice.
If swallowed	• Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything to an unconscious person. • Call a poison control center or physician for treatment advice.
If inhaled	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. • Call a poison control center or doctor for further treatment advice
NOTE TO PHYSICIAN:	
Probable mucosal damage may contraindicate the use of gastric lavage.	
HOTLINE NUMBER:	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For Chemical Emergency, Spill Leak, Fire Exposure or Accident, Call CHEMTREC Day or Night Domestic North America 800-424-9300 International 703-527-3883 (collect calls accepted).	

EPA Reg. No. 82283-2
EPA Est. No. 39108-CHN-001
Net Contents: 45 gallons (200 liters)
(Net contents: 45 gallons will be placed on the container)

DOMINUS is a trademark of Isagro USA, Inc.

BIOPESTICIDES REGISTRATION ACTION DOCUMENT

Oil of Mustard and Ally Isothiocyanate (ATIC)

PC Code: 004901

U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division

(last updated September 11, 2013)

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BIOPESTICIDES REGISTRATION ACTION DOCUMENT (BRAD) TEAM

Branch Chief
Linda A. Hollis, M.S.

Product Chemistry/Human Health Effects/Nontarget Organisms
Russell Jones, Ph.D., Senior Scientist

Regulatory Action Leader
Gina Burnett, M.S.

I. EXECUTIVE SUMMARY

Allyl isothiocyanate (AITC) is a naturally occurring component of Oil of Mustard, which was first registered by the Agency for pesticidal use in 1962. As part of Oil of Mustard, AITC has been determined by the Agency to be the residue of concern and, as such, has been well characterized in the Reregistration Eligibility Decision for Flower and Vegetable Oils (EPA, 1993), the Biopesticides Registration Action Document for Oriental Mustard Seed (PC Code 014921) (EPA, 2008), and the Vegetable and Flower Oil Summary Document for Registration Review (EPA, 2010). AITC is produced naturally when enzymes of the mustard plant, myrosinase and glucosolinate, are in the presence of water. In addition to its presence in mustard, AITC can be found in food commodities such as cooked cabbage, kale, and horseradish. It is synthetically produced from allyl iodide and potassium thiocyanate. In pesticidal products, AITC is used as an insect and animal repellent, feeding suppressant, insecticide, fungicide, herbicide and nematicide.

Currently, pesticide product (MP), IR9804 (EPA File Symbol No. 89285-R) and end-use product (EP), IRF135 (EPA File Symbol 89285-E), are proposed to be registered. These products contain synthetic AITC at 99.8% and 96.3%, respectively. IRF135 is intended for use as an insecticide, fungicide, herbicide and nematicide to be applied (1) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, (2) by drip injection, also covered by tarp overlay, and (3) by deep injection to depths greater than 17 inches, with no tarp covering. IR9804 is intended for formulation into end-use products for soil treatment. The currently proposed label application methods are for pre-plant applications, which would be considered a non-food use. No residual activity is expected and the active ingredient and its degredates will dissipate prior to crop seeding.

The Agency has concluded that adequate mammalian toxicology data are available to support AITC (EPA, 1993; EPA 2010). The oral LD_{50} in rats is 339 mg/kg (EPA, 1993). Human exposure to AITC is expected to be minimal from the proposed MP and soil treatment EP, IR9804 (EPA File Symbol No. 89285-R) and IRF135 (EPA File Symbol 89285-E) (EPA, 2013). The active ingredient is not likely to result in adverse human health effects, based upon available reports and information.

AITC rapidly degrades in the environment by normal biological, physical and/or chemical processes that can be reasonably expected to exist where the pesticide is applied (EPA, 2013). In each case of registration of products containing AITC, sufficient data or information has been submitted to demonstrate that there will be no toxicity or adverse effects to nontarget organisms with the exception of certain insects and honey bees (EPA, 2008). The Agency has concluded that the honey bee toxicity issue can be appropriately addressed thru end-use product label mitigation.

On October 1, 2009, the U.S. Environmental Protection Agency (EPA or the Agency) announced a policy to provide a more meaningful opportunity for the public to participate in major registration decisions before they occur. According to this policy, EPA provides a public comment period prior to making a registration decision for the following types of applications: new active ingredients; first food uses; first outdoor uses; first residential uses; or any other

registration actions for which EPA believes there may be significant public interest.

Consistent with the policy of making registration decisions more transparent, the public is being provided 15 days in which to submit comments to the Agency regarding its pending decision to register products containing AITC for use as a pre-plant soil treatment. The following documents are available for comment in the docket, identification number EPA-HQ-OPP-2013-0658: a draft of this Biopesticides Registration Action Document (BRAD), the draft product labels for IR9804 (EPA File Symbol 89285-R) and IRF135 (EPA File Symbol 89285-E), and the Agency science review memorandum for these products (EPA, 2013). **Note: The draft EP label will be revised, during this period, to include additional mitigation measures in accordance with those seen for similar application methods (soil fumigants) but as appropriate for this biopesticide. Intended revisions will include (1) an entry restricted period section on the label, (2) a fumigant management plan section, (3) clarification of restrictions for workers verses handlers, and (4) clarification of methods to determine soil and weather conditions.**

Altogether, the Agency believes that, based on the existing information in the Agency's database on AITC and the recent information submitted in support of the registration of pesticide products containing AITC for pre-plant soil treatment, it is in the best interest of the public to issue the registrations for IR9804 (EPA File Symbol 89285-R) and IRF135 (EPA File Symbol 89285-E). The basis for this decision can be found in the science review memorandum for these products (EPA, 2013) and the existing information in the Agency's database on AITC, both of which are characterized in this BRAD.

For definitions of scientific terms, please refer to *http://www.epa.gov/pesticides/glossary/*.

II. ACTIVE INGREDIENT OVERVIEW

Common Name:	Oil of Mustard
Chemical Names:	1-Propene, 3-isothiocyanato- 2-Propenyl isothiochyanate 3-Isothiocyanato-1-propene Allyl isosulfocyanate Allyl isothiocyanate Allyl mustard oil
Trade & Other Names:	Oil of Mustard Allyl isothiocyanate (AITC)
CAS Registry Number:	57-06-7
OPP Chemical Code:	004901
Type of Pesticide:	Biochemical Pesticide – insect and animal repellent, feeding suppressant, insecticide, fungicide, herbicide and nematicide

Biochemical Classification

Oil of Mustard, containing the residue of conern AITC, was first approved by the Agency for use in a registered product as a biochemical insecticide in 1962. For more information regarding product chemistry data requirements, please refer to Tables 1 thru 4 in Appendix A for this document.

III. REGULATORY BACKGROUND

A. Application for Pesticide Registration

On August 29, 2012, Technology Sciences Group, Inc., on behalf of Isagro USA, Inc. (hereafter referred to as "Isagro" or "applicant"), 430 Davis Drive, Suite 240, Morrisville, NC, 27560, submitted applications to register a new biochemical pesticide products, IR9804 (EPA File Symbol 89285-R) and IRF135 (EPA File Symbol 89285-E), containing AITC as their active ingredient. IRF135 is intended for use as an insecticide, fungicide, herbicide and nematicide to be applied to be applied (1) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, (2) by drip injection, also covered by tarp overlay, and 3) by deep injection to depths greater than 17 inches, with no tarp covering. IR9804 is intended for formulation into end-use products for soil treatment.

B. Food Clearances/Tolerances

AITC is exempt from the requirement of a tolerance as stated at 40 CFR § 180.1167:

> **40 CFR § 180.1167 Allyl isothiocyanate as a component of food grade oil of mustard; exemption from the requirement of a tolerance.**
>
> The insecticide and repellent Allyl isothiocyanate is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling.

The proposed end-use product, IRF135 (EPA File Symbol 89285-E), is labeled for pre-plant soil application only. The active ingredient (synthetic AITC) and its degradates will dissipate prior to planting. The Agency considers this to be a non-food use and, therefore, a tolerance or exemption from the requirement of a tolerance is not required.

IV. RISK ASSESSMENT

A. Product Analysis Assessment (40 CFR § 158.2030)

Biochemical pesticide product analysis data requirements include product chemistry and composition, analysis and certified limits, and physical and chemical characteristics. Product chemistry and composition data include information about the identity of the active ingredient, the manufacturing process, and discussion of the potential for formation of unintentional ingredients. Analysis and certified limits data include information on analysis of samples and certification of limits. Physical and chemical characteristics data describe basic characteristics of

the registered pesticide products, including color, physical state, odor, stability, miscibility, pH, corrosion characteristics, viscosity and density.

All product chemistry data requirements have been satisfied for the active ingredient (Oil of Mustard/AITC) and the proposed products, IR9804 (EPA File Symbol 89285-R) and IRF135 (EPA File Symbol 89285-E). Refer to Tables 1 thru 4 in Appendix A for a summary of product chemistry data specific to these products. Refer to the Vegetable and Flower Oil Summary Document for Registration Review (EPA, 2010) for a summary of product chemistry information for Oil of Mustard/AITC.

B. Human Health Assessment

1. Tier I Toxicology

AITC has already been assessed by the Agency and the Agency has concluded that adequate mammalian toxicology data are available to support this biochemical pesticide (EPA, 1993; EPA, 2008; EPA 2010). In addition, adequate mammalian toxicology data and information are available to support registration of IR9804 (EPA File Symbol No. 89285-R) and IRF135 (EPA File Symbol 89285-E). This information is summarized below and listed in Table 5 in Appendix A of this document.

Acute Toxicity for IR9804 (EPA File Symbol 89285-R) and IRF135 (EPA File Symbol 89285-E) ***(OCSPP Guideline Nos. 870.1100, 870.1200, 870.1300, 870.2400, 870.2500, and 870.2600; Master Record Identification (MRID) Nos. 488241-03 thru -07):***

The acute oral toxicity in rats for IF9804 (EPA File Symbol 89285-R), containing 99.8% AITC, is LD_{50} = 425.4 mg/kg. Acute dermal toxicity (rat) is LD_{50} > 200 mg/kg, and acute inhalation toxicity (rat) is LC_{50} > 0.21 mg/L. Therefore, IR9804 (EPA File Symbol 89285-R) is categorized as Toxicity Category II for acute oral toxicity, acute dermal toxicity, and acute inhalation toxicity. It is categorized as Toxicity Category I for primary eye irritation and primary dermal irritation due to its corrosivity, and is classified as a dermal sensitizer. No hypersensitivity incidents have been reported.

Guideline studies for acute human health toxicity testing were not submitted for the EP, IRF135 (EPA File Symbol 89285-E). In lieu of Guideline studies, the applicant submitted a request to bridge the acute toxicity data submitted in support of the TGAI/MP (containing 99.8% AITC) to support the acute toxicity data requirements for the EP (containing 96.5% AITC). The Agency has determined this request to be acceptable based upon the substantial similar formulation between these two products.

Subchronic Toxicity, Developmental Toxicity, and Mutagenicity Testing for IR9804 (EPA File Symbol No. 89285-R) (Tier I) ***(OCSPP Guideline Nos. 870.3100, 870.3250, 870.3465; 870.3700, 870.5100, 870.5300, 870.5375; MRID No. 48824108):***

A Guideline 90-day oral toxicity study was not submitted. In lieu of a study, the applicant cited a 90-day oral toxicity study conducted by the National Toxicology Program (NTP, 1982) on

F344/N rats dosed with 1.5 to 25 mg AITC/kg-body wgt/day, five days per week for 13 weeks which had a No Observed Adverse Effect Level (NOAEL) of 25 mg AITC/kg-body wgt/day, the highest level tested. No mortalities occurred during the course of the study and no treatment-related effects were observed on tissues obtained from the test animals when compared to non-treated controls. There were no differences in body weights between treated animals and non-treated controls (EPA, 2013).

A Guideline 90-day dermal toxicity study was not submitted. The applicant requested and was granted a waiver based on the fact that the product is not intended for application to human skin and prolonged or repeated dermal contact is not expected when EPs for pre-plant soil treatment are applied in accordance with Agency approved use directions and PPE (for handlers: coveralls worn over long sleeve shirt and long pants, chemical resistant footwear plus socks, chemical resistant gloves, protective eyewear, and an air purifying respirator). Similarly, a Guideline 90-day inhalation toxicity study was not submitted. The applicant requested and was granted a waiver based on the fact that repeated inhalation exposure to AITC aerosol, vapor or gas is highly unlikely and not expected, when the EPs for pre-plant soil treatment is applied in accordance with EPA approved label use directions and PPE.

A Guideline Prenatal Developmental Toxicity study was not submitted. In lieu of a study, the applicant cited a study in which AITC was one of 16 chemically-related compounds evaluated in order to correlate potential developmental toxicity with molecular structure. In this study, no difference in the percentage of abnormal fetuses in AITC-treated offspring were detected compared to control, and no difference between treated and control in the percentage of dead fetuses was detected. The authors concluded that AITC did not display any teratogenic potential at the NOAEL of 60 mg/kg. The 60 mg/kg dose would be equivalent to 4.2 g AITC for a standard 70 kg human (EPA, 2013).

Guideline Mutagenicity studies were not submitted. In lieu of a study, the applicant cited a battery of mutagenicity studies on AITC conducted by the National Toxicology Program (NTP). In this battery, two reverse mutation studies confirmed that mutagenicity responses were negative in all strains tested with and without S9 activation. In three *in vitro* mammalian gene mutation studies, a negative response was observed in the first trial using mouse lymphoma cells without S9 activation at concentrations ranging from 0.05 to 0.8 mg/mL AITC. A second trial without S9 exhibited a significant increase in average mutant frequency and significant reduction in relative total growth at AITC concentrations of 0.4, 0.6, and 0.8 mg/mL; 1.0 mg/mL was cytotoxic. A third trial without S9 also exhibited a significant increase in average mutant frequency at concentrations of 0.6 to 1.4 mg/mL and a significant reduction in growth; a concentration of 1.6 mg/mL was cytotoxic. It is noted that the positive results were observed without S9 activation and in the presence of substantial cytotoxicity. An *in vivo* mammalian chromosome aberration study was conducted with mice dosed intraperitoneally with 0, 25, or 50 mg/kg AITC and compared against mice dosed with a positive control, dimethylbenzanthracine (DMBA). Increases in chromosome aberrations were not observed in AITC treated mice when compared to non-treated (negative) controls, while a positive response was observed in DMBA-treated mice. The Agency has determined that the weight of evidence demonstrates that AITC is not likely to be a mutagen. In addition, the method of application and rapid degradation rate for the proposed pre-plant soil treatment, together with appropriate PPE, mitigates exposure to

humans (EPA, 2013).

2. Tier II and Tier III Toxicity Studies

The biochemical pesticide Human Health Assessment data requirements for Tier II and Tier III were not required due to the low toxicity of the active ingredient and the low levels of exposure expected from its intended uses in EP products.

3. Effects on the Endocrine System

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA issued test orders and data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and nine inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

AITC (as contained in Oil of Mustard) is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders and data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier 1 screening battery, please visit our website: http://www.epa.gov/endo/.

4. Dose Response Assessment

No toxicological endpoints have been identified for Oil of Mustard or AITC; therefore, a dose-response assessment was not required.

5. Drinking Water Exposure and Risk Characterization

No significant exposure from drinking water is expected when products containing Oil of

Mustard or AITC are used according to the product label directions. AITC is a naturally occurring component of the human diet and degrades rapidly in the soil with a short half-life (T½) ranging from 20 to 60 hours. AITC transforms in sterilized soil at the same rate as intact soil, indicating that degredation is not dependent on soil microbial populations. Products containing AITC will not be directly applied to water. However, in an aqueous solution in the pH range between 6 and 8, AITC is proposed to degrade completely. Within this pH range, the primary decomposition products identified were: allyl thiocyanate (ATC); allylamine (AA); and carbon disulfide (CDS). ATC, an isomer of AITC, was identified at each pH and sampling interval; AA is expected to biodegrade quickly in the environment, and so if it is formed following AITC treatment of soil, human and animal exposure is unlikely. CDS is naturally occurring in the environment, and is released from tree roots, tidal marshes and soil. CDS is considered ubiquitous in the environment, and so formation of carbon disulfide from treating soil with AITC would not increase exposure to non-target organisms over levels currently in the environment (EPA, 2013).

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

a. Occupational Exposure and Risk Characterization

Occupational exposure to the proposed soil treatment EP, IRF135 (EPA File Symbol 89285-E), is not expected due to mitigation through precautionary language and personal protective equipment (PPE) on the label.For other products containing AITC, the Agency has required labels to include the appropriate signal word and precautionary statements, as PPE if applicable, to mitigate any risk of exposure.

b. Residential, School and Day Care Exposnre and Risk Characterization

The proposed soil treatment EP, IRF135 (EPA File Symbol 89285-E), is for agricultural use only. Previously approved AITC products for outdoor residential use have been approved by the Agency based on minimal exposure to AITC when used according to label directions. No indoor residential, school, or day care uses are currently approved for products containing AITC.

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

There is reasonable certainty of no harm to U.S. populations, including infants and children, from aggregate exposures to residues of AITC when used as proposed. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. Moreover, potential non-occupational inhalation and dermal exposure is not likely to pose any adverse effects to exposed populations via aggregate and cumulative exposure.

a. Food Exposure

Dietary exposure of AITC is already occurring, given that this substance can be found in many foods commonly consumed by humans such as cooked cabbage, kale, horseradish, and mustard. AITC is exempt from the requirement of a tolerance for residues when used as a component of

food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling. Furthermore, the proposed use of synthetic AITC as a pre-plant soil treatment will not result on residues on food as the AITC, and its degradates, will readily degrade prior to planting (EPA, 2013).

b. Drinking Water Exposure

The proposed use of synthetic AITC as a pre-plant soil treatment will not result in water residues because this biochemical degrades rapidly in the soil with a short half-life (T½) ranging from 20 to 60 hours. Products containing AITC will not be directly applied to water. However, in an aqueous solution in the pH range between 6 and 8, AITC is proposed to degrade completely. Therefore, drinking water exposure from the proposed used pattern is not expected to pose incremental risk to adults, infants and children via drinking water consumption.

c. Other Non-occupational Exposure

The proposed soil treatment EP, IRF135 (EPA File Symbol 89285-E), is for agricultural use only. Previously approved AITC products for outdoor residential use have been approved by the Agency based on minimal exposure to AITC when used according to label directions. Other non-occupational use is not expected for products containing this active ingredient.

8. Cumulative Effects from Substances with a Common Mechanism of Toxicity

AITC has no demonstrated subchronic toxicity; thus, there is no reason to expect cumulative effects of exposure to Pear Ester and to other substances with common mechanism of toxicity.

9. Determination of Safety for United States Population, Infants and Children

AITC is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling. Therefore, it is expected that no harm will result from aggregate exposure to the United States population, including infants and children, to the residues of AITC on food commodities. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. Thus, there are not threshold effects of concern and consequently, provisions requiring additional margin of safety do not apply. Furthermore, the proposed use of synthetic AITC as a pre-plant soil treatment will not result on residues on food as the AITC, and its degradates, will readily degrade prior to planting (EPA, 2013).

10. Risk Characterization

The Agency considered human exposure to AITC in light of the relevant safety factors in FQPA and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the use of products containing AITC when label instructions are followed.

C. Environmental Assessment

1. Ecological Hazards

Oil of Mustard and AITC have already been assessed by the Agency and the Agency has concluded that adequate nontarget organism toxicology data and information are available to support these ingredients (EPA, 1993; EPA, 2008; EPA 2010). In addition, adequate nontarget organism toxicology data information were to support registration of IR9804 (EPA File Symbol No. 89285-R) and IRF135 (EPA File Symbol 89285-E). This information is summarized in Table 6, in Appendix A of this document.

2. Environmental Fate and Ground Water Data

Environmental fate and groundwater data are not required at this time because the results of the nontarget organism toxicity assessment (Tier I data requirements) did not trigger these Tier II data requirements.

3. Ecological Exposure aud Risk Characterization

Exposure and risk from the registered and proposed (pre-plant soil treatment) uses of AITC are expected to be minimal for nontarget organisms, with the exception of honey bees (EPA, 2013). Exposure to honey bees will be mitigated by appropriate label language on end-use products.

4. Endangered Species Assessment

The Agency believes that Oil of Mustard and AITC will have "No Effect" on any currently listed threatened and endangered species, or any designated critical habitat, as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Oceanic and Atmospheric Administration's (NOAA) National Marine Fisheries Service (NMFS) (EPA, 2010). EPA anticipates conducting no further analysis of potential risks to endangered or threatened species unless public comments during the Registration Review process alter the Agency's current position. The Registration Review for these active ingredients is ongoing as of the date of this document, September, 2013.

D. Product Performance Data

Product performance (efficacy) data must be developed for all pesticides to ensure that the products will perform as intended and that unnecessary pesticide exposure to the environment will not occur as a result of the use of ineffective products. The Agency reserves the right to require, on a case-by- case basis, the submission of efficacy data for any pesticide product registered or proposed for registration, but applications to register pesticide products intended to control a pest of significance public health importance, as defined in FIFRA section 28(d) and section 2(nn), must include such data. For further guidance on the product performance data requirement, refer to Pesticide Registration Notice (PR) Notices 96-7, 2002-1 and Explanation of Statutory Framework for Risk-Benefit Balancing for Public Health Pesticides (http://www.epa.gov/PR_Notices/pr1996-7.pdf) (http://www.ea.gov/PR_Notices/pr2002-1.pdf) and (http://www.epa.gov/pesticides/health/risk-benefit.htm).

Oil of Mustard and AITC are not intended to be formulated into products to control public health pests as defined in FIFRA section 28(d) and section 2(nn), and product performance (efficacy) was not evaluated by the Agency.

V. RISK MANAGEMENT DECISION

A. Determination of Eligibility for Registration

Section 3(c)(5) of FIFRA provides for pesticide product registration if it is determined that: (A) its composition warrants proposed claims; (B) its labeling and other materials comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment.

The four eligibility criteria have been satisfied for the proposed pesticide products containing the active ingredient AITC (and for all previous registered pesticide products containing AITC and Oil of Mustard).

B. Regulatory Decision

The data submitted fulfill the requirements for the unconditional registration IR9804 (EPA File Symbol No. 89285-R) as an MP to be formulated into soil treatment products and IRF135 (EPA File Symbol 89285-E) as an EP for pre-plant soil treatment. For these product labels and for product-specific labels and information on other product containing Oil of Mustard and AITC, please refer to http://www.epa.gov/pesticides/pestlabels.

C. Environmental Justice

EPA seeks to achieve environmental justice—the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income—with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. At this time, EPA does not believe that products containing the active ingredients Oil of Mustard or AITC, or the use of AITC for pre-plant soil treatment will cause harm or a disproportionate impact on at-risk communities. For additional information regarding environmental justice issues, please visit EPA's website at *http://www.epa.gov/compliance/environmentaljustice/index.html*.

VI. ACTIONS REQUIRED BY REGISTRANTS

EPA evaluated all data submitted in connection with the registration of AITC for pre-plant soil treatment and determined that these data are sufficient to satisfy current registration data requirements. At this time, no additional data must be submitted to EPA for these particular products. For new uses and/or changes to existing uses, EPA may require additional data. Notwithstanding the information stated in the previous paragraph, it should be clearly understood that certain specific data are required to be reported to EPA as a requirement for maintaining the federal registration for a pesticide product. A brief summary of these types of data are listed

below.

A. Reporting of Adverse Effects

Pursuant to FIFRA section 6(a)(2), reports of all incidents of adverse effects to the environment must be submitted to EPA.

B. Reporting of Hypersensitivity Incidents

Under the provisions of 40 CFR Part 158.2050(d), all incidents of hypersensitivity (including both suspected and confirmed incidents) must be reported to the Agency.

VII. Appendix A. Data Requirements (40 CFR Part 158-Subpart U)

TABLE 1. Product Chemistry Data Requirements for 1R9804 (99.8% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Study**	**Results**	**MRID**
830.1550 to 830.1670	Product identity; Manufactnring process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities. **ACCEPTABLE**	48824101
830.1700	Analysis of samples	Submitted data satisfy the requirements for analysis of samples. **ACCEPTABLE**	48824102
830.1750	Certification of limits	Limits listed in the CSF are **ACCEPTABLE**	-
830.1800	Analytical method	**ACCEPTABLE**	48824102

TABLE 2. Physical and Chemical Properties of IR9804 (99.8% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID**
830.6302	Color	Colorless or pale yellow liquid	48824101
830.6303	Physical State	Liquid	48824101
830.6304	Odor	Very pungent, irritating aroma	48824101
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Reported stable.	48824101
830.6315	Flammability	Flashpoint = 46°C	48824101
830.6317	Storage Stability	Study in progress – anticipated completion date is the last quarter of 2013.	48824101
830.6319	Miscibility	Not Applicable; TGAI/MP is not an emulsifiable liquid and is not diluted with petroleum solvents.	-
830.6320	Corrosion Characteristics	Study in progress – anticipated completion date is the last quarter of 2013.	48824101
830.7000	pH	4-5	48824101
830.7050	UV/Visible Light Absorption	Refractive index 1.524-1.531; see http://www.fao.org/ag/agn/jefca-flav/img/img/1560.gif for the absorbance spectrum	48824101
830.7100	Viscosity	Not Applicable for TGAI/MP	-
830.7200	Melting Point/Range	-102.5°C	48824101
830.7220	Boiling Point/Range	150-151°C; 148-154°C	48824101
830.7300	Density	1.013-1.020; 1.0	48824101
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not Applicable; TGAI/MP is not fibrous	-
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Log P = 2.11	48824101
830.7840	Water Solubility	Slightly soluble in water	48824101
830.7950	Vapor Pressure	1.33 kPa @ 38.3°C 0.493 kPa@ 20°C	48824101

TABLE 3. Product Chemistry Data Requirements for IRF135 (96.3% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Study**	**Results**	**MRID Method/Refereuce**
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities. **ACCEPTABLE**	489194-01
830.1700	Analysis of samples	Not required for EP	489194-02
830.1750	Certification of limits	Limits listed in the CSF are **ACCEPTABLE**	489194-01
830.1800	Analytical method	Not required for EP	489194-02

TABLE 4. Physical and Chemical Properties of IRF135 (96.3% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID**
830.6302	Color	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6303	Physical State	Liquid	489194-01
830.6304	Odor	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6315	Flammability (flashpoint)	47°C	489194-02
830.6317	Storage Stability	Study in progress– anticipated completion date is the last quarter of 2013.	489194-01
830.6319	Miscibility	Not applicable per 40 CFR 158.2030(e)(10) – EP is not an emulsifiable liquid and is not to be diluted with petroleum solvents.	-
830.6320	Corrosion Characteristics	Study in progress– anticipated completion date is the last quarter of 2013.	489194-01
830.7000	pH	4.87 (1% soln)	489194-02
830.7050	UV/Visible Light Absorption	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7100	Viscosity	0.6 centistokes @ 40°C 0.8 centistokes @ 20°C	489194-02
830.7200	Melting Point/Range	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7220	Boiling Point/Range	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7300	Density	1.019 g/mL @ 20°C	489194-02
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7840	Water Solubility	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7950	Vapor Pressure	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-

Table 5. Mammalian Toxicology Data Requirements for IR9804 (EPA File Symbol 89285-R) (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	LD_{50} = 425.4 mg/kg **ACCEPTABLE**	II	488241-03
Acute dermal toxicity (rat) (870.1200)	LD_{50} > 200 mg/kg **ACCEPTABLE**	II	488241-04
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 0.21 mg/L **ACCEPTABLE**	II	488241-05
Primary eye irritation (rabbit) (870.2400)	Waiver due to observed corrosiveness on skin **ACCEPTABLE**	I	1
Primary dermal irritation (rabbit) (870.2500)	Corrosive **ACCEPTABLE**	I	488241-06
Dermal sensitization (guinea pig) (870.2600)	Sensitizer **ACCEPTABLE**	-	488241-07
Hypersensitivity incidents (885.3400)	-	-	-
90-Day oral toxicity (870.3100)	Rationale submitted **ACCEPTABLE**		488241-08
90-Day dermal toxicity (870.3250)	Rationale submitted **ACCEPTABLE**		488241-08
90-Day inhalation toxicity (870.3465)	Rationale submitted **ACCEPTABLE**		488241-08
Mutagenicity (870.5100, 5300 and 5375)	Rationale submitted **ACCEPTABLE**		488241-08
Developmental toxicity (870.3700)	Rationale submitted **ACCEPTABLE**		488241-08

Table 6. Non-Target Organism Data Requirements for IR9804 (EPA File Symbol 89285-R) (40 CFR § 158.2060)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Avian Acute Oral/OPPTS 850.2100	Rationale submitted **ACCEPTABLE**	No acute oral exposure based on application method and rapid environmental degradation	48824108, p. 18
Avian Dietary/OPPTS 850.2200	Rationale submitted **ACCEPTABLE**	No dietary exposure based on application method and rapid environmental degradation	48824108, p. 20
Freshwater Fish LC50/OPPTS 850.1075	Rationale submitted 96-hr LC_{50} = 0.077 ppm **ACCEPTABLE**	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 22, 37-47
Freshwater Invertebrate/OPPTS 850.1010	Rationale submitted 48-hr EC_{50} = 0.73 ppm **ACCEPTABLE**	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 23, 216-221
Non-target Plants/OPPTS 850.4100 & 4150	Rationale submitted **ACCEPTABLE**	No non-target exposure based on application method and rapid environmental degradation	48824108, pp. 24-27
Non-target Insects	Rationale submitted **ACCEPTABLE**	No non-target exposure based on application method and rapid environmental degradation	48824108, pp. 28, 29

VIII. Appendix B. References

1. U.S. EPA, 1993. Registration Eligibility Decision (RED). Flower and Vegetable Oils. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). December 1, 1993. Available at: http://www.epa.gov/opp00001/chem_search/reg_actions/reregistration/red_G-114_01-Dec-93.pdf

2. U.S. EPA, 2008. Oriental Mustard Seed (PC Code 014921). Biopesticides Registration Action Document. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). December 17, 2008. Available at: http://www.epa.gov/pesticides/chem_search/reg_actions/registration/decision_PC-014921_17-Dec-08.pdf

3. U.S EPA, 2010. Vegetable and Flower Oils Summary Document. Registration Review: Initial Docket. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). March 29, 2010. Available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0904-0005

4. U.S. EPA, 2013. Memorandum from Russel Jones, Ph.D. to Gina Burnett. Science Review in Support of the Registration of the TGAI/MP IR9804 and the EP, IRF 135, Respectively Containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) As Their Active Ingredient. The TGAI/MP is an unregistered source of the active ingredient. Office of Pesticide Programs. U.S. Environmental Protection Agency (U.S. EPA). May 15, 2013.

IX. GLOSSARY OF ACRONYMS AND ABBREVIATIONS

a.i.	active ingredient
BPPD	Biopesticides and Pollution Prevention Division
BRAD	Biopesticide Registration Action Document
bw	body weight
CBI	Confidential Business Information
CFR	Code of Federal Regulations
cm^3	cubic centimeter
CSF	Confidential Statement of Formula
°C	degrees Celsius
EC_{50}	median effective concentration. A statistically derived single concentration in environmental medium that can be expected to cause an effect in 50% of the test animals when administrated by the route indicated (inhalation). It is expressed as a concentration in air or water (e.g. mg/L).
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EP	end-use product
EPA	Environmental Protection Agency (the "Agency")
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	Food Quality Protection Act
FR	Federal Register
g	gram
ha	hectare
kg	kilogram
Kow	octanol-water partition coefficient
L	liter
LC_{50}	median lethal concentration. A statistically derived single concentration in air or water that can be expected to cause death in 50% of the test animals when administrated by the route indicated (inhalation and environment). It is expressed as a concentration in air or water (e.g. mg/L).
LD_{50}	median lethal dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral and dermal). It is expressed as a weight of substance per unit weight of animal (e.g., mg/kg).
MRID No.	Master Record Identification Number
mg	milligram
mPa	millipascal
mL	milliliter
MP	manufacturing-use product
N/A	not applicable
NE	"No Effect"
NIOSH	National Institute for Occupational Safety and Health

nm	nanometer
NOEL	no-observed-effect-level
NOF	notice of filing
NOR	notice of receipt
OPP	Office of Pesticide Programs
OCSPP	Office of Chemical Safety and Pollution Prevention
pa	pascal
PPE	personal protective equipment
PR Notice	Pesticide Registration Notice
TGAI	technical grade of the active ingredient
ug	microgram
USDA	United States Department of Agriculture
UV	ultra-violet

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Office of Chemical Safety and Pollution Prevention

MEMORANDUM **May 15, 2013**

SUBJECT: Science Review in Support of the Registration of the TGAI/MP IR9804 and the EP, IRF 135, Respectively Containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) As Their Active Ingredient. The TGAI/MP is an unregistered source of the active ingredient.

Decision No :	469288 & 469289
DP Nos.:	406246 & 406248
EPA Reg. Nos:	89285-R & -E
Chemical Class:	Biochemical
CAS. No.:	57-06-7
PC Code:	004901
Tolerance Exemptions :	40 CFR 180.1167 (for AITC) in Oil of Mustard
MRID Nos. :	488241-01 to -08 & 489194-01 to -03

FROM: Russell S. Jones, Ph.D, Senior Biologist /S/ 05/15/2013
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Gina Burnett, Regulatory Action Leader /S/ 05/15/2013
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

On behalf of Isagro, A. Roberts (TSG) submitted a request for the registration of the TGAI/MP IR9804 and the EP, IRF 135, respectively containing 99.8% and 96.3% Allyl Isothiocyanate (AITC) as their active ingredient. The TGAI/MP is an unregistered source of the active ingredient. In support of the submission, the registrant has submitted Product Chemistry and Tier I Toxicity information and waivers for all Tier I Non-Target Organism data requirements.

Under 40 CFR 180.1167 Allyl isothiocyanate is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling. The inert ingredient is cleared for food use under 40 CFR 180.910.

The currently proposed label application methods are for pre-plant applications, which would be considered a non-food use. No residual activity is expected and the active ingredient will dissipate prior to crop seeding.

RECOMMENDATIONS AND CONCLUSIONS

1a. The Product Chemistry data submitted in support of the TGAI/MP, IR9804 (EPA File Symbol No. are 89285-R), are **ACCEPTABLE.**

1b. The Product Chemistry data submitted in support of the EP, IRF135 (EPA File Symbol No. are 89285-E), are **ACCEPTABLE.**

2a. The Tier I Toxicity studies, data, and waiver rationales submitted in support of the TGAI/MP data requirements are **ACCEPTABLE.** No additional data are required.

2b. Tier I Toxicity information submitted in support of the TGAI/MP is bridged to support of the EP data requirements. **ACCEPTABLE.**

3. Waiver rationales submitted in support of the TGAI/MP Non-Target Organism data requirements are **ACCEPTABLE.**

STUDY SUMMARIES

I. Active Ingredient Characterization

Allyl isothiocyanate (AITC) is the major component of natural mustard oil. It is present also in cooked cabbage, horseradish, and black mustard seed. It is synthetically produced from allyl iodide and potassium thiocyanate

Product Names: TGAI/MP: IR9804 (99.8% a.i.) (EPA File Symbol No. 89285-R)
EP: IRF135 (96.3% a.i.) (EPA File Symbol No. 89285-E)

Chemical Name:	Allyl isothiocyanate
Common Names:	AITC, 3-Isothiocyanato-1-propene
PC Code:	070704
CAS No.:	56-06-7
Molecular Wgt.:	99.15
Chemical Formula:	C_4H_5NS

See MRID 48824101, pp. 5 & 6, and Attachment 1 for additional details on IR9804.
See MRID 48919401, pp. 5, and Attachment 1 for additional details on IRF135.

A. Product Chemistry (MRIDs 488241-01 & -02; 489194-01 & -02)

Data submitted to support the product chemistry data requirements for the TGAI/MP (IR9804; EPA File Symbol No. 89285-R) are summarized in Table 1 below. Physical and chemical properties data are summarized in Table 2 below. Refer to MRIDs 488241-01 and -02 for more information.

TABLE 1. Product Chemistry Data Requirements for TGAI/MP IR9804 (99.8% AITC) (40 CFR § 158.2030)

OPPTS Guideline No.	Study	Results	MRID
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities. **ACCEPTABLE**	48824101
830.1700	Analysis of samples	Submitted data satisfy the requirements for analysis of samples. **ACCEPTABLE**	48824102
830.1750	Certification of limits	Limits listed in the CSF are **ACCEPTABLE**	-
830.1800	Analytical method	**ACCEPTABLE**	48824102

TABLE 2. Physical and Chemical Properties of TGAI/MP IR9804 (99.8% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID Method/Reference**
830.6302	Color	Colorless or pale yellow liquid	48824101 JECFA (2005) – see Attachment 1 [1]
830.6303	Physical State	Liquid	48824101 JECFA (2005) – see Attachment 1 [1]
830.6304	Odor	Very pungent, irritating aroma	48824101 JECFA (2005) – see Attachment 1 [1]
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Reported stable.	48824101 EPA-HQ-OPP-2009-0904 – Vegetable and Flower Oils Summary Document for Registration Review – March 2012
830.6315	Flammability	Flashpoint = 46°C	48824101 International Chemical Safety Card, CDC/NIOSH (1997) – see Attachment 1
830.6317	Storage Stability	Study in progress – anticipated completion date is the last quarter of 2013.	48824101 Per method of analysis used in OCSPP 830.1800.
830.6319	Miscibility	Not Applicable; TGAI/MP is not an emulsifiable liquid and is not diluted with petroleum solvents.	-
830.6320	Corrosion Characteristics	Study in progress – anticipated completion date is the last quarter of 2013.	48824101 Visual inspection of packaging materials during a one-year storage stability study.
830.7000	pH	4-5	pH meter
830.7050	UV/Visible Light Absorption	Refractive index 1.524-1.531; see http://www.fao.org/ag/agn/jefcu-flav/img/img/1560.gif for the absorbance spectrum	48824101 JECFA (2005) – see Attachment 1 [1]
830.7100	Viscosity	Not Applicable for TGAI/MP	-
830.7200	Melting Point/Range	-102.5°C	48824101 International Chemical Safety Card, CDC/NIOSH (1997) – see Attachment 1
830.7220	Boiling Point/Range	150-151°C 148-154°C	48824101 JECFA (2005) – see Attachment 1 [1] International Chemical Safety Card, CDC/NIOSH (1997) – see

TABLE 2. Physical and Chemical Properties of TGAI/MP IR9804 (99.8% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID Method/Reference**
			Attachment 1
830.7300	Density	1.013-1.020 1.0	48824101 JECFA (2005) – see Attachment 1 [1] International Chemical Safety Card, CDC/NIOSH (1997) – see Attachment 1
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not Applicable; TGAI/MP is not fibrous	-
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Log P = 2.11	48824101 IARC Monograph Volume 73 – see Attachment 1
830.7840	Water Solubility	Slightly soluble in water	48824101 JECFA (2005) – see Attachment 1 [1]
830.7950	Vapor Pressure	1.33 kPa @ 38.3°C 0.493 kPa@ 20°C	48824101 IARC Monograph Volume 73 – see Attachment 1 International Chemical Safety Card, CDC/NIOSH (1997) – see Attachment 1

Classification: ACCEPTABLE

Data submitted to support the product chemistry data requirements for the EP (; EPA File Symbol No. 89285-E) are summarized in Table 3 below. Physical and chemical properties data are summarized in Table 4 below. Refer to MRIDs 489194-01 and -02 for more information.

TABLE 3. Product Chemistry Data Requirements for EP IRF135 (96.3% AITC) (40 CFR § 158.2030)

OPPTS Guideline No.	Study	Results *(below are example results)*	MRID Method/Reference
830.1550 to 830.1670	Product identity; Manufacturing process; Discussion of formation of unintentional ingredients	Submitted data satisfy the requirements for product identity, manufacturing process, and discussion of formation of impurities. **ACCEPTABLE**	489194-01
830.1700	Analysis of samples	Not required for EP	489194-02
830.1750	Certification of limits	Limits listed in the CSF are **ACCEPTABLE**	489194-01
830.1800	Analytical method	Not required for EP	489194-02

TABLE 4. Physical and Chemical Properties of EP IRF135 (96.3% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID**
830.6302	Color	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6303	Physical State	Liquid	489194-01 Visual inspection at room temperature
830.6304	Odor	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6313	Stability to Normal and Elevated Temperatures, Metals and Metal Ions	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.6315	Flammability (flashpoint)	47°C	489194-02 Pensky-Martens Closed Cup
830.6317	Storage Stability	Study in progress– anticipated completion date is the last quarter of 2013.	489194-01 Per method of analysis used in OCSPP 830.1800.
830.6319	Miscibility	Not applicable per 40 CFR 158.2030(e)(10) – EP is not an emulsifiable liquid and is not to be diluted with petroleum solvents.	-
830.6320	Corrosion Characteristics	Study in progress– anticipated completion date is the last quarter of 2013.	489194-01 Visual inspection of packaging materials during a one-year storage stability study.
830.7000	pH	4.87 (1% soln)	489194-02 pH meter
830.7050	UV/Visible Light Absorption	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7100	Viscosity	0.6 centistokes @ 40°C 0.8 centistokes @ 20°C	489194-02 ASTM D445/D446 Test Methods and OPPTS 830.7100
830.7200	Melting Point/Range	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7220	Boiling Point/Range	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7300	Density	1.019 g/mL @ 20°C	489194-02 CIPAC MT-3, ASTM D891-95, OPPTS 830.7300 and OECD TG 109
830.7520	Particle Size, Fiber Length and Diameter Distribution	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7550 830.7560 830.7570	Partition Coefficient (n-Octanol/Water)	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-
830.7840	Water Solubility	Not applicable per 40 CFR 158.2030(e) – Product is an	-

TABLE 4. Physical and Chemical Properties of EP IRF135 (96.3% AITC) (40 CFR § 158.2030)			
OPPTS Guideline No.	**Property**	**Description of Result**	**MRID**
		EP.	
830.7950	Vapor Pressure	Not applicable per 40 CFR 158.2030(e) – Product is an EP.	-

Classification: ACCEPTABLE

II. Human Health Assessment

A. Toxicology for TGAI/MP (MRID 48824108)

The data presented in Table 5 below are a summary of the toxicity data and information submitted to support the TGAI/MP . Refer to the DERs for more information.

Table 5. Mammalian Toxicology Data Requirements for TGAI/MP AITC (40 CFR § 158.2050)			
Study/OPPTS Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	LD_{50} = 425.4 mg/kg **ACCEPTABLE**	II	488241-03
Acute dermal toxicity (rat) (870.1200)	LD_{50} > 200 mg/kg **ACCEPTABLE**	II	488241-04
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 0.21 mg/L **ACCEPTABLE**	II	488241-05
Primary eye irritation (rabbit) (870.2400)	Waiver due to observed corrosiveness on skin **ACCEPTABLE**	I	1
Primary dermal irritation (rabbit) (870.2500)	Corrosive **ACCEPTABLE**	I	488241-06
Dermal sensitization (guinea pig) (870.2600)	Sensitizer **ACCEPTABLE**	-	488241-07
Hypersensitivity incidents (885.3400)	-	-	-
90-Day oral toxicity (870.3100)	Rationale submitted **ACCEPTABLE**		488241-08
90-Day dermal toxicity (870.3250)	Rationale submitted **ACCEPTABLE**		488241-08
90-Day inhalation toxicity (870.3465)	Rationale submitted **ACCEPTABLE**		488241-08
Mutagenicity (870.5100, 5300 and 5375)	Rationale submitted **ACCEPTABLE**		488241-08
Developmental toxicity (870.3700)	Rationale submitted **ACCEPTABLE**		488241-08

1. Acute Toxicity for the TGAI/MP IR9804 (99.8%; EPA File Symbol No. 89285-R)

The AITC technical (EPA Reg. No. 89285-R; 99.8% a.i.) is in Toxicity Category II for acute oral toxicity, acute dermal toxicity, and acute inhalation toxicity. It is in Toxicity Category I for primary eye irritation and primary dermal irritation due to its corrosivity. No hypersensitivity incidents have been reported.

NOTE: All references cited in the following discussions of the rationales submitted in support of the Tier I data requirements may be found in the respective sections of MRID 48824108. Similarly, more detailed discussions of Methods and Materials used in the cited studies may be found in MRID 48824108 or in the cited studies themselves.

2. Subchronic Toxicity

90-Day Oral Toxicity in Rodents (OCSPP 870.3100): A Guideline 90-day oral toxicity study was not submitted. In lieu of a study, the applicant submitted a rationale to support the data requirement. The rationale is based on the following:

a. A 90-day oral toxicity study conducted by the National Toxicology Program (NTP, 1982) on F344/N rats dosed with 1.5 to 25 mg AITC/kg-body wgt/day, five days per week for 13 weeks had a No Observed Adverse Effect Level (NOAEL) of 25 mg AITC/kg-body wgt/day, the highest level tested. No mortalities occurred during the course of the study and no treatment-related effects were observed on tissues obtained from the test animals when compared to non-treated controls. There were no differences in body weights between treated animals and non-treated controls.

b. Humans are regularly exposed to AITC in the diet, and to sinigrin, a precursor to AITC, which is converted to AITC by the enzyme, myrosinase, upon disruption of cells. AITC and sinigrin are present at relatively high levels in cauliflower, kale, horseradish, wasabi, and mustard. For example, Wasabi contains up to 34 umol of sinigrin/AITC per gram and brown mustard has been shown to contain approximately 0.453 mg AITC per gram. The official serving size of Grey Poupon Dijon mustard (according to the product label) is one teaspoon, which is equal to 5 grams, equivalent to 2.27 mg AITC/serving (Bhattacharya et al., 2010; Jiao et al., 1994; & Zhang, 2010).

c Oral exposure to AITC when used as a soil-applied pesticide is not expected to increase above normal dietary exposure in foods due to the rapid degradation of AITC in soil and water. AITC degradation in soil has been reported to be rapid with a half-life ranging from 20 to 60 hours, with a mean half-life of 47 hours ($\pm$ 27) in six different soil types. Degradation is greatest in soils with high organic matter (OM) and total nitrogen (N) content, and increases with increasing temperature. Up to 97.1% AITC degrades within 10 days at 20 ^{o}C in high OM and N soils (Borek et al., 1995; & Pechacek et al., 1997).

d. The primary degradation products of AITC in moist soils are likely to be allyl thiocyanate (ATC), allylamine (AA), and carbon disulfide, (CDS) based on experiments using AITC in

aqueous solution at varying temperatures (20-80 °C for 80 minutes) and pH levels pH 6-8). ATC, an isomer of AITC, was identified at each pH level tested and is expected to degrade as rapidly as AITC. Likewise, the chemically similar AA, if it is formed, is expected to degrade quickly. CDS is already present in the environment and is released to terrestrial soils via exudates from tree roots, and is present in tidal marshes. Increased oral exposure to AITC degradates via application of AITC to soils is unlikely based on natural occurrence and the environmental fate of these compounds (HSDB, 2012; & Pechacek et al., 1997).

e. In addition, the Agency notes that the proposed end-use product is intended for use as a pre-plant soil treatment . The product label specifies that the soil applied product be permitted to completely dissipate from the treated soil prior to the planting of any crop (as determined by lettuce seed and/or tomato/pepper transplant bioassays. The presence of residues on edible commodities, as well as oral dietary exposure to AITC are highly unlikely.

CLASSIFICATION: ACCEPTABLE

90-Day Dermal Toxicity (OCSPP 870.3250): A Guideline 90-day dermal toxicity study was not submitted. In lieu of a study, the applicant submitted a rationale to support the data requirement. The rationale is based on the following:

a. The proposed end-use product is intended for use as a pre-plant soil treatment.

b. The product is not intended for application to human skin.

c. Prolonged or repeated dermal contact is not expected when the EP is applied in accordance with label use directions. The application methods are: (i) tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, (ii) by drip injection, also covered by tarp overlay, and (iii) by deep injection to depths greater than 17 inches, with no tarp covering. These application methods minimize the potential for dermal exposure.

d. In addition, the Agency notes that the product label specifies a 48-hour re-entry interval unless wearing appropriate PPE (coveralls, protective eyewear, chemical resistant gloves, and footwear plus socks). Repeated dermal exposure to the pre-plant soil applied end-use product is highly unlikely.

CLASSIFICATION: ACCEPTABLE

90-Day Inhalation Toxicity (OCSPP 870.3465): A Guideline 90-day dermal toxicity study was not submitted. In lieu of a study, the applicant submitted a rationale to support the data requirement. The rationale is based on the following:

a. Repeated inhalation exposure to AITC aerosol, vapor or gas is highly unlikely and not expected, when the EP is applied in accordance with label use directions. The application methods are: (i) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by

tarp overlay, (ii) by drip injection, also covered by tarp overlay, and 3) by deep injection to depths greater than 17 inches, with no tarp covering. These application methods minimize the potential for inhalation exposure.

b. AITC degrades readily in soil and water and, therefore, inhalation exposure is highly unlikely to occur after the tarps are removed following treatment (Borek et al., 1995; Pecháček et al., 1997). AITC degrades rapidly in the soil with a short half-life (T½) ranging from 20 to 60 hours (Borek et al., 1995). The average T½ of AITC in six different soil types was reported to be 47 ± 27 hours, with the greatest degradation rate of in soils that have high organic carbon and total nitrogen (N) content. In addition, the AITC T½ in soil increases with increasing moisture content and decreases in soil with increasing temperature between 10°C and 25°C. During the first 24 hours, an average of 29.8% of AITC was transformed, or degraded, and over the first 10 days at 20°C, an average of 97.1% was degraded (Borek et al., 1995). The data also demonstrate that AITC transforms in sterilized soil at the same rate as intact soil, indicating that microbial populations are not responsible for the degradation (Borek et al., 1995). The more rapid degradation that occurs in soil with higher levels of organic carbon suggests that AITC reacts with the organic material and is inactivated. The rapid degradation of AITC in treated soil suggests that inhalation exposure will be highly unlikely following pre-plant soil treatments in accordance with label use directions.

c. The metabolism of AITC has been described in evaluations of food and food additives, and is not expected to be any different following inhalation exposure than following oral exposure. AITC is metabolized in humans by conjugation with glutathione and this conjugate is further metabolized to mercapturic acids that are eliminated via the urine (Shapiro et al., 1998). The available data suggest that AITC is metabolized via the same pathways regardless of the route of exposure.

d. Based on the information discussed above in paragraph "c," acute and subchronic oral toxicity data may be used to characterize the potential risk from inhalation exposure to AITC. A 90-Day Oral Toxicity study with AITC that provided a no-observed-adverse-effect-level (NOAEL) of 25 mg/kg/day has been conducted (NTP, 1982). AITC was administered to rats by gavage at doses of 0, 1.5, 3, 6, 12, and 25 mg/kg/day for 13-weeks. Any AITC inhalation exposure identified may be compared to an acceptable exposure level identified based on the NOAEL from this study.

CLASSIFICATION: ACCEPTABLE

3. Developmental Toxicity (OCSPP 870.3700): A Guideline Prenatal Developmental Toxicity study was not submitted. In lieu of a study, the applicant submitted a rationale to support the data requirement. The rationale is based on the following:

a. Allyl Isothiocyanate (AITC) was one of 16 chemically-related compounds evaluated in a study designed to correlate potential developmental toxicity with molecular structure (Ruddick et al., 1976). In this study, a single dose of AITC was administered to pregnant dams at 60 mg/kg or 120 mg/kg by gavage on day 12 or 13 of gestation and the dams were

sacrificed on day 22 and examined for individual litter weight, litter size, and number of deciduomas and corpora lutea. Control animals were administered equivalent doses of either water or corn oil. The results were compared against pregnant dams dosed with the suspected teratogen, ethylenethiourea (ETU). The higher dose was close to the LD_{50} for AITC, so only results at the lower dose were used. No difference in the percentage of abnormal fetuses in AITC-treated offspring were detected compared to control, and no difference between treated and control in the % dead fetuses was detected. The authors concluded that AITC did not display any teratogenic potential at the NOAEL of 60 mg/kg. The 60 mg/kg dose would be equivalent to 4.2 g AITC for a standard 70 kg human.

b. Human dietary exposure to AITC is common due to natural occurrence of AITC in many foods. Many vegetables contain AITC or produce the precursor to AITC, sinigrin, which is converted by the enzyme myrosinase to AITC upon disruption of the cells (Bhattacharya et al., 2010; Zhang, 2010) and upon exposure to moisture. Sinigrin and/or AITC levels are typically high in cauliflower, kale, horseradish, wasabi and mustard. Wasabi may contain up to 34 µmol sinigrin / AITC per gram (Zhang 2010), whereas brown mustard has been shown to contain approximately 0.453 mg of AITC per gram, such that a 10 gram serving contains 4.53 mg of AITC (Jiao et al., 1994). The official serving size for Grey Poupon Dijon mustard identified on the label is one teaspoon, which is equal to 5 grams (2.27 g AITC equivalent or 0.54x of the NOAEL)

c. See discussion under part "b." of the 90-day Inhalation rationale above. In addition, possible degradation products of AITC in soil can be proposed based on the decomposition products of AITC present in an aqueous solution in the pH range between 6 and 8, where AITC is proposed to degrade completely (Pecháček et al., 1997). Within this pH range, Pecháček et al. (1997) observed that the primary decomposition products identified at 80 °C and in lower quantities at 20 °C and 40 °C after an 80 min incubation, were: allyl thiocyanate (ATC); allylamine (AA); and carbon disulfide (CDS). ATC, an isomer of AITC, was identified at each pH and sampling interval; AA is expected to biodegrade quickly in the environment, and so if it is formed following AITC treatment of soil, human and animal exposure is unlikely (HSDB). CDS is naturally occurring in the environment, and is released from tree roots, tidal marshes and soil (HSDB). CDS is considered ubiquitous in the environment, and so formation of carbon disulfide from treating soil with AITC would not increase exposure over levels currently in the environment (HSDB, accessed 8/2012).

d. Application methods together with appropriate PPE will mitigate human exposure. The application methods are: (i) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, (ii) by drip injection, also covered by tarp overlay, and 3) by deep injection to depths greater than 17 inches, with no tarp covering. These application methods minimize the potential for inhalation exposure.

Human exposure to the primary degradates of AITC identified in aqueous solutions following soil treatment in the environment appears unlikely based on the natural occurrence and environmental fate of these compounds, as well as the methods of application

CLASSIFICATION: ACCEPTABLE

4. Mutagenicity (OCSPP 870.5100; 870.5300; & 870.5375): Guideline Mutagenicity studies were not submitted. In lieu of a study, the applicant submitted a rationale to support the data requirements. The rationale is based on the following:

a. The National Toxicology Program (NTP) has conducted a battery of mutagenicity studies (NTP, 1981, 1988, & 1991) on AITC, including a Bacterial Reverse Mutation Assay using *S. typhimurium* strains TA100, TA1535, and TA99 with and without S9 activation; and *In Vitro* Mammalian Gene Mutation Test using mouse lymphoma L5178Y TK+/- cells; and an *In Vivo* Mammalian Chromosome Aberration Test.

b. Two reverse mutation studies (NTP, 1981) confirmed that mutagenicity responses were negative in all strains tested with and without S9 activation.

c. Three *in vitro* mammalian gene mutation studies were conducted using mouse lymphoma cells without S9 activation (NTP, 1988). A negative response was observed in the first trial using mouse lymphoma cells without S9 activation at concentrations ranging from 0.05 to 0.8 mg/mL AITC. A second trial without S9 exhibited a significant increase in average mutant frequency and significant reduction in relative total growth at AITC concentrations of 0.4, 0.6, and 0.8 mg/mL; 1.0 mg/mL was cytotoxic. A third trial without S9 also exhibited a significant increase in average mutant frequency at concentrations of 0.6 to 1.4 mg/mL and a significant reduction in growth; a concentration of 1.6 mg/mL was cytotoxic. It is noted that the positive results were observed without S9 activation and in the presence of substantial cytotoxicity.

d. An *in vivo* mammalian chromosome aberration study (NTP, 1991) was conducted with mice dosed intraperitoneally with 0, 25, or 50 mg/kg AITC and compared against mice dosed with a positive control, dimethylbenzanthracine (DMBA). Increases in chromosome aberrations were not observed in AITC treated mice when compared to non-treated (negative) controls, while a positive response was observed in DMBA-treated mice.

e. The weight of evidence demonstrates that AITC is not likely to be a mutagen. In addition, the method of application and rapid degradation rate, together with appropriate PPE, mitigates exposure to humans.

CLASSIFICATION: ACCEPTABLE

B. Toxicology for EP (MRID 488919103)

Guideline studies for acute toxicity testing were not submitted. In lieu of Guideline studies, the registrant submitted a request to bridge the acute toxicity data submitted in support of the TGAI/MP (containing 99.8% AITC) to support the acute toxicity data requirements for the EP (containing 96.5% AITC) [redacted]

Conclusions: The concentration of AITC is slightly lower in the EP (96.5%) than in the TGAI/MP (99.8%). [redacted] The bridging of acute toxicity data submitted in support of the TGAI/MP registration to support the registration of the EP, is acceptable.

CLASSIFICATION: ACCEPTABLE

III. Nontarget Organism Assessment (MRID 48824108)

The data presented in Table 6 below are a summary of the nontarget organism toxicity data and information submitted to support of the TGAI/MP. Refer to the appropriate pages in MRID 48844108 for more detailed information and specific reference citations from the scientific literature. .

Table 6. Non-Target Organism Data Requirements for TGAI/MP AITC (40 CFR § 158.2060)

Study/OPPTS Guideline No.	Results	Toxicity Category/Description	MRID
Avian Acute Oral/OPPTS 850.2100	Rationale submitted **ACCEPTABLE**	No acute oral exposure based on application method and rapid environmental degradation	48824108, p. 18
Avian Dietary/OPPTS 850.2200	Rationale submitted **ACCEPTABLE**	No dietary exposure based on application method and rapid environmental degradation	48824108, p. 20
Freshwater Fish LC50/OPPTS 850.1075	Rationale submitted 96-hr LC_{50} = 0.077 ppm **ACCEPTABLE**	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 22, 37-47
Freshwater Invertebrate/OPPTS 850.1010	Rationale submitted 48-hr EC_{50} = 0.73 ppm **ACCEPTABLE**	Very Highly Toxic, but no aquatic exposure based on application method and rapid environmental degradation	48824108, pp. 23, 216-221
Non-target Plants/OPPTS 850.4100 & 4150	Rationale submitted **ACCEPTABLE**	No non-target exposure based on application method and rapid environmental degradation	48824108, pp. 24-27
Non-target Insects	Rationale submitted **ACCEPTABLE**	No non-target exposure based on application method and rapid environmental degradation	48824108, pp. 28, 29

SUMMARY:

Guideline studies were not submitted in support of the non-target organism data requirements. In lieu of Guideline studies, the applicant submitted rationales, on a Guideline-by-Guideline basis, for each non-target organism data requirement, which were supported both by scientific

literature citations as well as an argument for a lack of exposure to non-target organisms to AITC based on its rapid degradation in soil, its widespread presence in commonly eaten foods, as well as by the methods and timing of application of the EP.

AITC degrades readily in soil and water and, therefore, inhalation exposure is highly unlikely to occur after the tarps are removed following treatment (Borek et al., 1995; Pecháček et al., 1997). AITC degrades rapidly in the soil with a short half-life (T½) ranging from 20 to 60 hours (Borek et al., 1995). The average T½ of AITC in six different soil types was reported to be 47 ± 27 hours, with the greatest degradation rate of in soils that have high organic carbon and total nitrogen (N) content. In addition, the AITC T½ in soil increases with increasing moisture content and decreases in soil with increasing temperature between 10°C and 25°C. During the first 24 hours, an average of 29.8% of AITC was transformed, or degraded, and over the first 10 days at 20°C, an average of 97.1% was degraded (Borek et al., 1995). The data also demonstrate that AITC transforms in sterilized soil at the same rate as intact soil, indicating that microbial populations are not responsible for the degradation (Borek et al., 1995). The more rapid degradation that occurs in soil with higher levels of organic carbon suggests that AITC reacts with the organic material and is inactivated. The rapid degradation of AITC in treated soil suggests that inhalation exposure will be highly unlikely following pre-plant soil treatments in accordance with label use directions.

In addition, possible degradation products of AITC in soil can be proposed based on the decomposition products of AITC present in an aqueous solution in the pH range between 6 and 8, where AITC is proposed to degrade completely (Pecháček et al., 1997). Within this pH range, Pecháček et al. (1997) observed that the primary decomposition products identified at 80 °C and in lower quantities at 20 °C and 40 °C after an 80 min incubation, were: allyl thiocyanate (ATC); allylamine (AA); and carbon disulfide (CDS). ATC, an isomer of AITC, was identified at each pH and sampling interval; AA is expected to biodegrade quickly in the environment, and so if it is formed following AITC treatment of soil, human and animal exposure is unlikely (HSDB). CDS is naturally occurring in the environment, and is released from tree roots, tidal marshes and soil (HSDB). CDS is considered ubiquitous in the environment, and so formation of carbon disulfide from treating soil with AITC would not increase exposure to non-target organisms over levels currently in the environment (HSDB, accessed 8/2012).

IRF135 is an end-use product (EP) formulated from IR9804, which is a technical grade active ingredient (TGAI/MP) containing 99.8% allyl isothiocyanate (AITC). IRF135 is approximately 96.5% AITC and 3.5% of a well known surfactant approved for food use under 40 CFR 180.910. IRF135 is intended for use in an as a pre-plant soil treatment to control and repel fungi, insects, nematodes and weeds. AITC is a component of many common cruciferous vegetables including broccoli and Brussels sprouts, and is particularly concentrated in mustard seed, horseradish, and wasabi.

Application methods together with appropriate PPE will mitigate human exposure. The application methods are: (i) by tractor mounted shank injection at a depth of 8 to 15 inches, followed by tarp overlay, (ii) by drip injection, also covered by tarp overlay, and 3) by deep injection to depths greater than 17 inches, with no tarp covering. These application methods minimize the potential for exposure to non-target organisms.

CLASSIFICATION: ACCEPTABLE

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division (7511P)
1200 Pennsylvania Avenue NW
Washington, DC 20460

NOTICE OF PESTICIDE:
X Registration
___ Reregistration
(under FIFRA, as amended)

EPA Reg. Number:	Date of Issuance:
89285-2	

Term of Issuance: **Unconditional**

Name of Pesticide Product:

IRF135

Name and Address of Registrant (include ZIP Code):

Amy Plato Roberts
Isagro USA, Inc
P.O. Box 990
Hailey, ID 83333

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Biopesticides and Pollution Prevention Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This registration does not eliminate the need for continual reassessment of the pesticide. If EPA determines at any time that additional data are required to maintain in effect an existing registration, the Agency will require submission of such data under section 3(c)(2)(B) of FIFRA. This product is unconditionally registered in accordance with FIFRA Sec. 3(c)(5) provided you:

1. Submit and/or cite all data required for registration of your product under FIFRA section 3(c)(5) when the Agency requires all registrants of similar products to submit such data.

2. Revise the EPA Registration Number to read, "EPA Reg. No. 89285-2."

3. Submit two (2) copies of the final printed labeling before you release the product for shipment. Refer to the A-79 enclosure for a further description of final printed labeling.

A stamped copy of the label is enclosed for your records.

Signature of Approving Official:	Date:
Robert McNally, Director, Biopesticides and Pollution Prevention Division	9/26/13

EPA Form 8570-6

IRF135

ACCEPTED
SEP 26 2013
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 89285-2

(Alternate Brand Name: "DOMINUS®")

Biopesticide for Agricultural Soil Treatment Use

A BROAD SPECTRUM PRE-PLANT SOIL BIOFUMIGANT FOR THE CONTROL OF CERTAIN SOIL BORNE FUNGI, NEMATODES, WEEDS and INSECTS

ACTIVE INGREDIENT:	
Allyl isothiocyanate	96.3%
OTHER INGREDIENTS:	3.7%
TOTAL:	100.0%

Contains 8.19 lbs. active ingredient (allyl isothiocyanate) per gallon. This product weighs 8.5 lbs. per gallon.

KEEP OUT OF REACH OF CHILDREN
DANGER

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail).

FIRST AID	
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, and then continue rinsing. • Call a poison control center or physician for treatment advice.
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15 minutes. • Call a poison control center of doctor for treatment advice.
If swallowed	• Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything to an unconscious person. • Call a poison control center or physician for treatment advice.
If Inhaled	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. • Call a poison control center or doctor for further treatment advice
NOTE TO PHYSICIAN	
Probably mucosal damage may contraindicate the use of gastric lavage.	
HOTLINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For Chemical Emergency Spill Leak Fire Exposure or Accident Call CHEMTREC Day or Night Domestic North America 800-424-9300 International 703-527-3883 (collect calls accepted).	

EPA Reg. No. (pending as File Symbol 89285-E) **EPA Est. No.** XXXXX-XXX-XXX
Net Contents:
(Batch Code/Lot No: *will be placed on the container*)
Manufactured for:
Isagro USA, Inc.
430 Davis Drive, Suite 240
Morrisville, NC 27560

Table of Contents

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

DANGER. Corrosive. Causes irreversible eye damage and skin burns. May be fatal if swallowed, absorbed through skin, or inhaled. Do not get in eyes, on skin or on clothing. Do not breathe vapor. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before use.

PERSONAL PROTECTIVE EQUIPMENT (PPE)

When performing activities without the potential for liquid contact all handlers (including applicators) must wear:

- Coveralls worn over long sleeve shirt and long pants
- Chemical-resistant footwear plus socks
- Chemical-resistant (such as nitrile or butyl) gloves
- Protective eyewear
- Respirator (see below)

Where liquid contact is a potential all handlers (including mixers, loaders and applicators) in addition to the above listed PPE must wear an air purifying respirator with an organic-vapor removing cartridge with pre-filter approved for pesticides (MSHA/NIOSH approval number prefix TC-23C), or a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or a NIOSH approved respirator with an organic vapor (OV) cartridge or canister with any N, R,

P or HE pre-filter.

When cleaning equipment, wear a chemical resistant apron.

Follow the manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry. Discard any clothing and or PPE that have been drenched or heavily contaminated with this product's concentrate. Do not reuse clothing or PPE that has been drenched or heavily contaminated.

ENGINEERING CONTROLS

When handlers use closed systems or enclosed cabs in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides, the handler PPE requirements may be reduced or modified as specified in the WPS at 40 CFR Part 170.

USER SAFETY RECOMMENDATIONS

- Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.
- Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

ENVIRONMENTAL HAZARDS

For terrestrial uses only. 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 when cleaning equipment or disposing of equipment wash water or rinsate.

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling. Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirement specific to your State or Tribe, consult the State/Tribal agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR Part 170. This standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. The requirements in this box apply to uses of this product that are covered by the Worker Protection Standard.

No instruction elsewhere on this labeling relieve user from complying with the requirements of the WPS.

For the entry restricted period and notification requirements, see the *Entry Restricted Period and Notification* section of this labeling. PPE for entry during the Entry Restricted Period that is permitted by this labeling is listed in the Personal Protective Equipment (PPE) section of this labeling.

Assure that labels and MSDS are on-site and readily available for employees to review.

ENTRY RESTRICTED PERIOD AND NOTIFICATION

Entry Restricted Period: Entry into the application block (including early entry that would otherwise be permitted under the WPS) by any person other than a correctly trained and PPE-equipped handler is PROHIBITED from the start of the application until 5 days after application is complete.

Notification: Notify workers of the application by warning them orally and by posting Biofumigant Treated Area signs. The sign must state:

1. "DANGER/PELIGROSO"
2. "Areas under (fumigation)(treatment). DO NOT ENTER/NO ENTRE"
3. Allyl Isothiocyanate biofumigant in use
4. Date and time of fumigation
5. Date and time entry restricted period is over
6. IRF135 and (*name of co-application*)
7. Name, address and telephone of applicator in charge

Post the Biofumigant Treated Area sign instead of the WPS sign for this application, but follow all WPS requirements pertaining to location, legibility, text size and sign size (40 CFR § 170.120).

Post Biofumigant Treated Area signs defining the fumigation buffer zone, at all entrances to the application block no sooner than 24 hours prior to application and remain in place until at least 24 hours from the start of the application; Signs placed at the corners or on the edges of the treated area must remain posted for at least 5 days (120 hours) from the start of the application, e.g. for no less than the duration of the entry restricted period.

TERMS USED IN THIS LABELING

Application Block: The area within the perimeter of the fumigated portion of a field (including furrows, irrigation ditches, and roadways). The perimeter of the application block is the border that connects the outermost edges of the total area treated with the biofumigant product.

Start of the Application: The time at which the biofumigant is first delivered/dispensed into the soil in the application block.

Application is Complete: The time at which the biofumigant has stopped being delivered/dispensed into the soil and the soil has been sealed; drip lines have been purged (if applicable).

Entry Restricted Period: This period begins at the start of the application and expires depending on the application method and if tarps are used when the tarps are perforated and removed. Entry into the application block during this period is only allowed for appropriately PPE-equipped handlers performing handling tasks. See the *Entry Restricted Period* and *Notification* sections of this label for additional information.

Buffer Zone: An area established around the perimeter of each application block. The buffer

zone must extend outward from the edge of the application block perimeter equally in all directions.

Buffer Zone Period: Begins at the start of the application and lasts for a minimum of 24-hours after the application is complete. Non-handlers must be excluded from the buffer zone during the buffer zone period.

Roadway: The portion of a street or highway improved, designed or ordinarily used for vehicular travel, exclusive of the sidewalk or shoulder even if such a sidewalk or shoulder is used by persons riding bicycles. In the event that a highway includes two or more seperated roadways, the term *roadway* shall refer to any such roadway separately.

PRODUCT INFORMATION
Apply IRF135 as a preplant soil treatment only and as a part of an integrated pest management (IPM) program to aid in reducing or controlling the damaging effects of soil borne pests and diseases.

USE PRECAUTION
The product must only be used in a well-ventilated area. Do not use IRF135 if it cannot be applied according to the use patterns on the label.

APPLICATIN WITH OTHER PRODUCTS
IRF135 may be applied with other pesticides or fertilizers by co-injection or co-application via the application methods outlined in this label. Consult specific product labels for additional information or restrictions concerning mix partner compatibility. Treat a small area first to ensure compatibility. Observe the most restrictive of the labeling limitations and precautions of all products used in mixtures.

SOIL TREATMENT APPLICATION METHODS
Apply as a preplant shank injection, broadcast/flat fume application, or raised bed application either shank injected into the row or in a raised bed or non-bedded strip injected through the drip irrigation system. Specific directions for each application method are provided below. Always follow label instructions to achieve optimum performance.

TARP REMOVAL, PERFORATION AND PLANTING INTERVAL
- Leave the soil undisturbed for at least 5 days after application is complete and prior to tarp cutting or perforation.
- For tarped applications, complete the cutting of the tarp or perforation/hole-punching 2 to 24 hours prior to tarp removal or planting to assist in IRF135 dissipation.
- Tarp cutters and removers shall wear long-sleeved shirt, long pants and gloves when removing tarps following application prior to planting.
- Cold, wet, or cold and wet soils can decrease dissipation of IRF135 and can require a longer soil exposure period.
- After application is complete, wait 10 days prior to planting.
- In addition to the 10 day waiting period, use of a Jar Seedling and/or Transplant tests for safety steps can be performed prior to planting the target crop. See page(s) 8-9 of this label for instructions.

SOIL TREATMENT TIMING AND APPLICATION RATES
- **Number of applications per year:** IRF135 may be applied to soil as a pre-plant soil

treatment prior to planting with subsequent applications allowable to the same soil within the same year provided the previous crop is completely harvested prior to application.

- **Open field:** Use 10 - 40 gallons of IRF135 per one acre (85 - 340 lb/A).
- **Greenhouse:** Use 10 - 40 gallons of IRF135 per one acre (85 - 340 lb/A) or 0.23 gal / 1,000ft^2 – 0.92 gal/1,000ft^2.

TABLE 1. PRE-PLANT SOIL APPLICATION RATES

TREATMENT SITE	BROADCAST EQUIVALENT RATES GAL/A*	BROADCAST EQUIVALENT RATES (LBS PRODUCT/A
Field soils to be planted to: Asparagus, brassica vegetables (broccoli, cauliflower), cereal grains, cucurbit crops (cucumber, squash, melons), fruiting vegetables (e.g. eggplant, peppers, tomatoes), herbs and spices, leek, leafy vegetables (lettuce), legume vegetables, pineapples, root and tuber vegetables (carrot, garlic, onion, potato, sweet potato)	10 - 40	85 - 340
Field soils to be planted to: Strawberries, berries (cane fruit) , fruit and nut crops, citrus, pome fruit trees, stone fruit trees, tree nuts, tropical and subtropical fruits, vineyards	10 - 40	85 - 340
Nursery, Turf, and Ornamental Soils to be planted to: Turf, lawns, parks, golf greens, athletic fields, recreational turf area, ornamentals, floral crops, forest tree seedlings	10 - 40	85 - 340
Greenhouse soils to be planted to: Food and Non-food crops	10 - 40	85 - 340
Seed or Transplant beds to be planted to:, Food crops and non-food crops	10 - 40	85 - 340
*Use the higher labeled rates for muck and heavy clay soils, as well as for those pests and or diseases such as cyst forming nematodes, *Macrophomina, Fusarium or Phytophthora* or hard coated weed seeds for example Malva, Clover or Nutsedge		

APPLICATION SITE CONDITION DIRECTIONS

Soil temperature: maximum of 90°F at a typical application depth

Soil preparation:

- Ensure the soil is well prepared and generally free at the surface of large clods. Large clods can prevent efficient soil sealing and reduce effectiveness of the product.
- Cultivate the soil to a minimum depth of 5-8" and/or equal to the desired treatment depth.

- Thoroughly incorporate plant residues into the soil to allow decomposition prior to treatment. Leave little or no plant residue present on the soil surface. Undecomposed plant material can harbor pests that will not be controlled and can interfere with the soil seal after application. Let crop residue that is present lie flat to permit the soil to be sealed effectively.
- Where applicable, fracture compacted soil layers (plow pans) within the desired treatment zone before or during application of IRF135.

Soil moisture:

- It is critical to maintain adequate soil moisture before, during and 48 hours post-treatment. Plan soil treatment for seasons, crop rotations, or irrigation schedules which leave adequate moisture in the soil.
- The soil must be moist (typically with enough moisture to allow weed seeds to become imbibed) from 1.5 inches below the soil surface to at least the minimum desired depth of the target treatment zone. The amount of moisture needed (typically greater than 50% Available Water Content at 9 inches) in this zone will vary according to soil type. Use the USDA Feel and Appearance Method (http://www.oneplan.org/Water/soilmoist.pdf) or a device that will accurately measure soil moisture. The surface soil generally dries very rapidly and is not considered in this determination.

Weather Conditions:

- Prior to soil treatment the weather forecast for the day of application and the 48-hour period following the soil treatment must be checked to determine if unfavorable weather conditions exist or are predicted (such as no wind speed or the potential for inversion layers) and whether soil treatment can begin.
- If significant rainfall occurs within 24 hours after IRF135 application (enough to saturate soil that has been treated with IRF135), a reduction in pest control can occur.
- Apply IRF135 in the presence of wind speeds of at least 2 mph at the start of the applications or projected to reach at least 5 mph during the application.
- Check weather forecasts 48 hours prior to application to ensure proper conditions are present at the time of application. Weather conditions and or advisories can be downloaded online at http://www.nws.noaa.gov.

Buffer Zones: Do not apply IRF135 within 25' of any occupied structure, such as a school, daycare, hospital, retirement home, business or residence.

PRE-PLANTING AFTER APPLICATION OF IRF135

Recontamination Prevention:

- IRF135 will control pests that are present in the soil treatment zone at the time of soil treatment. It will not control pests that are introduced into the soil after soil treatment period has ended. To avoid re-infestation of treated soil, DO NOT use irrigation water, transplants, seed pieces, or equipment that could carry soil-borne pests from infested land. Avoid contamination from moving infested soil onto treated beds through cultivation, movement of soil from outside the treated zone, dumping contaminated soil in treated fields and soil contamination from equipment or crop remains. Clean equipment carefully before entering treated fields.

Testing of Treated Soils Prior to Planting:

- Allow IRF135 to dissipate completely before planting the crop.

- When determining the appropriate time interval before planting, consideration of factors that impact IRF135 dissipation include rate of application, depth of injection, soil temperature, soil preparation and type, soil moisture and use of various plastic films and or water sealing.
- Use of a lettuce seed and or tomato/pepper transplant test can be used to determine if sufficient time has elapsed between soil treatment and planting as described below.

Lettuce Seed Test

- After a minimum of 7 days after application proceed with the following Seed Jar test.
- Use a trowel to dig into the treated soil to a depth at or just beneath the depth of IRF135 injection and remove 2 to 5 samples with enough soil to fill a quart sized jar half-way, mix lightly, apply moisture enough to germinate seeds, sprinkle seeds evenly over the soil surface and seal immediately with a lid for air tight conditions.
- Sample the field in several areas, especially those areas that are not representative of the general field conditions and or having higher moisture content, different soil texture or areas where rate delivery is different.
- Prepare another similar sample of untreated soil for comparison.
- Keep the jars out of direct sunlight and at a temperature of 65° to 85°F. (Direct sunlight can overheat and kill the seedlings). Lettuce seed will not germinate in the dark so place in diffuse sunlight.
- After 1 to 3 days, check each jar for seed germination.
- If seeds in the treated jar germinate and grow similar to the untreated soil sample then the treated area is safe for planting.

Tomato/Pepper Transplant Test

- After a minimum of 7 days after application proceed with the following transplant test.
- Transplant 5 to 10 healthy, actively growing tomato or pepper seedlings into treated beds at normal planting depth and several locations within the treated area. If available repeat in an area of field *not treated* with IRF135 for comparison. If a wetter, heavier area of the treated field is available place the transplants there.
- Inspect the transplants in 3 days for plant injury including wilt, chlorosis, or leaf and root tip burn. Ensure that proper soil moisture conditions exist for transplants to remain free from water stress. If plants in the treated area are asymptomatic and or are similar in growth and appearance to plants in the non-treated area it is safe to plant.

IRF135 DRIP (TRICKLE) CHEMIGATION APPLICATION USE DIRECTIONS:

Drip (Trickle) Chemigation Use Precautions:

- The following applies to drip (trickle) irrigation systems.
- Crop injury and a reduction in efficacy can result from non-uniform distribution of IRF135 in irrigation water used to treat soil.
- For questions related to equipment calibration, consult your local State Extension Service specialist, equipment manufacturer or dealer.

Soil preparation:

- Ensure compacted soil layers (plow pans) within the desired treatment zone are tilled and/or fractured if it is considered normal practice before application of IRF135 to ensure adequate soil drainage. Note that conditions where soil layers (plowpans) exist and are not tilled can result in reduced pest control, differences in planting interval or plant

growth as a result of compacted or shallow soil conditions.

- The application site must be in seedbed condition. Ensure beds are listed, shaped and ready for planting.
- Ensure initial soil moisture is at ~50% of field capacity at 2 to 3 inches and down to 9 inches depth at the time of IRF135 application. Soil texture and amount of water to be applied will impact the desired initial % field capacity necessary for drip injection.

IRF135 Dosage:

- Determining IRF135 dosage is based on consideration of the intended crop to be planted, treated area conditions, preparation, application method, target pest, and soil type.
- Use drip emitters with spacing of 4 to 12 inches with shallow subsurface placement to ensure thorough wetting of the soil area being treated by IRF135 drip injection.
- IRF135 must be metered at a target concentration between - 1000 – 3000 ppm (calculated by: total volume of product to be applied / total amount of water to be applied) x 1,000,000 into the water supply line and passed through a mixing device such as a centrifugal pump with by-pass agitation or static mixer to assure proper agitation and mixing to a target concentration (ppm) for even distribution before distribution into the drip irrigation system. The concentration of IRF135 should not exceed 3000 ppm at any time during the injection period within the drip line.
- The volume of irrigation water to deliver to the treated area is dependent upon the soil type, % soil moisture or the % of field capacity at the start of the application and the target moisture level following application and equipment rising.
- Determine the irrigation water flow and adjust the flow rate of IRF135 to meet the target ppm in irrigation water. Insert a static mixer or similar device immediately after the IRF135 injection point to insure adequate mixing with the irrigation water.

Chemigation Application Information:

1. Apply this product only through drip (trickle) irrigation systems. Do not apply this product through any other type of irrigation system.
2. Crop injury or lack of effectiveness can result from non-uniform distribution of treated water.
3. If you have questions about calibration, contact State Extension Service specialists, equipment manufacturers or other experts.
4. Do not connect an irrigation system (including greenhouse systems) used for pesticide application to a public water system unless the pesticide label-prescribed safety devices for public water systems are in place.
5. A person knowledgeable of the chemigation system and responsible for its operation or under the supervision of the responsible person, shall shut the system down and make necessary adjustments should the need arise.

Chemigation Systems Connected to Public Water Systems:

1. Public water system means a system for the provision to the public of piped water for human consumption if such system has at least 15 service connections or regularly serves an average of at least 25 individuals daily at least 60 days out of the year.
2. Chemigation systems connected to public water systems must contain a functional, reduced-pressure zone, back flow preventer (RPZ) or the functional equivalent in the water supply line upstream from the point of pesticide introduction. As an option to the RPZ, the water from the public water system should be discharged into a reservoir tank prior to pesticide introduction. There shall be a complete physical break (air gap)

between the flow outlet end of the fill pipe and the top or overflow rim of the reservoir tank of at least twice the inside diameter of the fill pipe.

Equipment Considerations for Drip (Trickle) Chemigation Systems:

1. The irrigation system (main line, headers, and drip tape) must be thoroughly inspected for leaks before the application starts. The leak detection process requires that the irrigations system be at full operating pressure. The time required at full operating pressure will vary according to the system design and layout, soil type and target ppm concentration. Signs of leaks may include puddling along major pipes and at the top or ends of rows and/or on the bed surface or movement or shifting of beds due to bed collapse in over saturated conditions. Any leaks discovered must be repaired prior to application of IRF135. For leaks discovered during application of IRF135, immediately stop injection, wear all appropriate PPE and repair the line insuring that the problem is corrected before commencing with the drip applied injection.
2. The system must contain a functional check valve (back flow prevention device), vacuum relief valve, and low pressure drain appropriately located on the irrigation pipeline to prevent water source contamination from back flow.
3. The pesticide injection pipeline must contain a functional, automatic, quick-closing check valve to prevent the flow of fluid back toward the injection pump.
4. With use of injection pumps (e.g. Diaphragm or Centrifugal type pumps) the pesticide injection pipeline must also contain a functional, normally closed, solenoid-operated valve located on the intake side of the injection pump and connected to the system interlock to prevent fluid from being withdrawn from the supply tank when the irrigation system is either automatically or manually shut down.
5. The system must contain functional interlocking controls to automatically shut off the pesticide injection pump when the water pump motor stops or in cases where there is no water pump, when the water pressure decreases to the point where pesticide distribution is adversely affected.
6. The irrigation line or water pump must include a functional pressure switch which will stop the water pump motor when the water pressure decreases to the point where pesticide distribution is adversely affected.
7. To inject IRF135, use a metering device (such as a positive pressure system, positive displacement injection pump, diaphragm pump, or a Venturi system) effectively designed and constructed of materials that are compatible with pesticides and capable of being fitted with a system interlock.
8. Use of an inert gas such as nitrogen or dry compressed air is acceptable for use in a positive pressure system.

Injection System Flush After IRF135 Application:

- **After IRF135 injection, continue drip irrigation with clean water to flush remaining IRF135 completely out of the system.** Apply 3 times the volume of water equivalent to the capacity of the drip injection system from the point of injection to the ends of the drip tape to ensure IRF135 is completely voided from the injection lines and drip tape.
- Do not allow any IRF135 to remain in the system after application.
- If common lines are used for both the IRF135 application and to apply the water seal (if applied), the lines must be adequately flushed before starting the water seal and/or normal irrigation practices.

Soil Sealing or Tarp Use:

- When tarps are used with drip injection application, they must be in place prior to

injection of IRF135.
- Tarp edges must be buried along the row furrow and at the ends of each row.

***Untarped* Drip (Trickle) Chemigation Applications:**
- Tarps must be used unless the drip tape is buried a minimum of 5 inches below the soil/air interface.

Planting Interval for Raised Bed Drip Applications:
- After application, leave the soil undisturbed for at least 10 days after the application is complete. Planting of the target crop is allowed at a minimum of 10 days following the completion of the application.
- Extremely cold, wet, or cold and wet soils can decrease dissipation of IRF135 and can require a longer soil exposure and/or aeration period.
- For tarped applications, where tarp perforation or hole punching occurs allow 2 to 24 hours aeration prior to planting to assist in IRF135 dissipation.
- Use of a Jar Seedling and/or Transplant test for crop safety can be performed prior to planting the target crop. See pages XX-XX of this label for instructions.

Requirements for Greenhouse Soil Treatment

- Applications methods for use in greenhouse soil treatment may be applied as drip injection or tractor mounted shank where applicable according to the methods described for open field with exceptions listed below:
  - All applications must be tarped or double water sealed (delivered via overhead sprinkler). Double water sealed is defined as twice the amount of water to deliver the soil treatment without causing over saturation of the soil or delivering enough water to maintain up to 80% soil moisture for 24 hours following application.
  - During the application, keep doors, vents and windows to the outside open and keep fans or other mechanical ventilation systems running within the application area.
  - Areas by which gases could enter adjacent enclosed areas must be sealed prior to application and remain closed for up to 48 hours post application.

IRF135 TRACTOR MOUNTED SHANK RAISED BED AND BROADCAST/FLAT FUME APPLICATION USE DIRECTIONS:

Soil moisture:
- For tractor mounted shank applied treatments of IRF135 do not apply to dry soils. Target a soil moisture reading of ~50% or greater Available Water Content to a depth of 8 to 9 inches present for at least 24 to 48 hours prior to and until the start of the application.

Soil temperature at application:
- Maximum of 90°F at application depth.

Application Methods and Equipment:
- Apply IRF135 using chisels spaced no more than 12 inches apart and no more than 3 outlets evenly spaced per chisel (rear and forward facing type shank). The top most outlets must be no less than 5 inches from the final air soil interface.
- For shank applications the use of tarps or a water cap does not eliminate the need to remove chisel traces. Use of a press board, ring roller or other device to effectively close

chisel traces must be performed.

Application Depth:

- The point of injection must be a minimum of 5 inches from the final soil/air interface. The point of deep injection must be at a minimum of 18 inches from the final soil/air interface. Use deeper placement when fumigating soil to be planted to deep-rooted plants, such as perennial fruit and nut crops, or to control deeply distributed pests.

Application Type	Injection depth	Single Sweep Chisel Spacing	Noble Plow Injector Outlet Spacing	Yetter Rig Injector Spacing	Tarped Type Sealing, Applied immediately after application*	Non-Tarped Type Sealing
Broadcast Shallow Shank	5 – 15 inches	6 – 12 inches Use of no more than 3 nozzles per sweep with 4-5 inches / nozzle and bottom nozzle at no more than 15 inches from soil surface	6 – 12 inches	4 – 6 inches	PE, VIF, TIF	Overhead sprinkler, water cap and/or Roller/Packer to compact soil surface, and close chisel traces
Broadcast Deep Shank	> 17 inches	18 – 24inches	NA	NA	NA	Roller/packer to compact soil surface
Raised Bed shallow shank or Strip Application	8 – 15 inches	6 – 12 inches Use of no more than 3 nozzles per sweep with 4 – 5 inches / nozzle and bottom nozzle at no more than 15 inches from soil surface	NA	4 – 6 inches	PE, VIF, TIF	Overhead Sprinkler, water cap and/or Roller/Packer to compact soil surface, and close chisel traces

* PE = Polyethylene film; VIF = Virtually Impermeable Film; TIF = Totally Impermeable Film

Prevention of End Row Spillage:

- Do not apply or allow IRF135 to spill onto the soil surface. Each injection line either needs a check valve located as close as possible to the soil injection point to avoid dripping or spillage. If a check valve system is not in place purge and drain the injection line prior to lifting the injection shanks from the ground.
- Only lift the injection shanks from the ground when the shut-off valve has been closed, and the IRF135 injection line has been depressurized to passively drain remaining IRF135 or when the system has been actively purged (e.g. via air compressor).

Injection Rig Calibration, Set-up, Repair, and Maintenance:

- IRF135 application equipment must be calibrated and all control systems working properly. Proper calibration is critical to ensure IRF135 application rate and soil placement. Refer to the equipment manufacturer's instructions to properly calibrate the injection equipment. The equipment dealer, local Cooperative Extension Service, crop advisor or IRF135 dealer can provide assistance.
- Flush all equipment with water after each day's use; disassemble valves and clean carefully. All rinsate should be properly applied to the field.

Planting Interval for Raised Bed Shank and Broadcast/Flat Fume Application

- After application, leave the soil undisturbed for at least 5 days after application prior to tarp cutting or perforation/hole punching.
- For tarped applications, complete cutting of the tarp for removal or perforation/hole punching 2 to 24 hours prior to tarp removal or planting to assist in IRF135 dissipation.
- Tarp cutters and removers shall wear long-sleeved shirt, long pants and gloves when there is no waiting or aeration period between tarp cutting and removing the tarp following application and prior to planting.
- Soil can be planted with the target crop at a minimum of 10 days following application.
- Cold, wet, or cold and wet soils can decrease dissipation of IRF135 and can require a longer soil exposure and or aeration period.
- Soil applied under untarped shanked applications must remain undisturbed for a minimum of 10 days following completion of the application before tillage and or planting of the target crop.
- Use of a Jar Seedling and/or Transplant test for crop safety can be performed prior to planting the target crop. See pages 8-9 of this label for instructions.

PESTS CONTROLLED FROM SOIL TREATMENT USES

Nematodes

Common Name (if applicable)	Scientific Name
Pin nematode	*Paratylenchus*
Ring nematode	*Mesocriconema* (=*Criconemoides*, =*Criconemella*)
Root knot nematode	*Meloidogyne*
Root-lesion nematode	*Pratylenchus*
Spiral nematode	*Helicotylenchus*
Sting nematode	*Belonolaimus*
Stubby-root nematode	*Paratrichodorus*
Stem and bulb nematode	*Tylenchus*

Soil Borne Fungi

Common Name (if applicable)	Scientific Name
Armillaria root rot	*Armillaria mellea*
Charcoal rot	*Macrophomina phaseolina*
Clubroot organism	*Plasmodiophora*
Corky root	*Pyrenochaeta*
Fusarium wilt	*Fusarium spp.*
Phytophthora	*Phytophthora spp.*
Pythium	*Pythium spp.*
Rhizoctonia	*Rhizoctonia spp.*
Southern blight	*Sclerotium rolfsii*
Verticillium wilt	*Verticillium dahliae*

Insects in the Soil at the Time of Treatment

Common Name (if applicable)	Scientific Name (if applicable)
Cutworms	
Japanese beetles	
June beetles and larva	
Symphylan (centipedes)	
White grubs	
Wireworms	

Weeds

Common Name (if applicable)	Scientific Name
California burclover	*Medicago lupulina*
Common chickweed	*Stellaria media*
Common mallow	*Malva neglecta*
Common purslane	*Portulaca oleracea*
Field bindweed	*Convolvulus arvensis*
Grasses	
Morningglory spp.	*Ipomoea spp.*
Prostrate knotweed	*Polygonum aviculare*
Yellow nutsedge	*Cyperus esculentus*

Mollusks: Slugs and Snails.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage and disposal.

PESTICIDE STORAGE
Store in original container in a cool, dry place.

PESTICIDE DISPOSAL
Waste resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

CONTAINER DISPOSAL for non-refillable containers
This is a non-refillable container. Do not reuse or refill this container. Empty the package

completely and triple rinse container (or equivalent pressure rinse) promptly after emptying with water to be used for application. Then dispose of the empty container according to state and local regulations. Place in trash or offer for recycling if available or return it to the Seller, or, if allowed by state and local authorities, by burning. If burned stay out of smoke.

TRIPLE RINSING INSTRUCTIONS:
For rigid, nonrefillable containers small enough to shake (with capacities equal to or less than 5 gallons):
Triple rinse as follows: Empty the remaining contents into application equipment or a mix tank and drain for 10 seconds after the flow begins to drip. Fill the container one-fourth full with water and recap. Shake for 10 seconds. Pour rinsate into application equipment or a mix tank or store rinsate for later use or disposal. Drain for 10 seconds after the flow begins to drip. Repeat this procedure two more times.

For rigid, non-refillable containers that are too large to shake (with capacities greater than 5 gallons):
Triple rinse as follows: Empty the remaining contents into application equipment or a mix tank. Fill the container one-fourth full with water. Replace and tighten closures. Tip container on its side and roll it back and forth, ensuring at least one complete revolution, for 30 seconds. Stand the container on its end and tip it back and forth several times. Turn the container over onto its other end and tip it back and forth several times. Empty the rinsate into application equipment or a mix tank or store rinsate for later use or disposal. Repeat this procedure two more times.

PRESSURE RINSE PROCEDURE (all sizes):
Pressure rinse as follows: Empty the remaining contents into application equipment or a tank mix and continue to drain for 10 seconds after the flow begins to drip. Hold container upside down over application equipment or mix tank or collect rinsate for later use or disposal. Insert pressure rinsing nozzle in the side of the container, and rinse at about 40 PSI for at least 30 seconds. Drain for 10 seconds after the flow begins to drip.

CONTAINER DISPOSAL for rigid, refillable containers
Refillable container. Refill this container with IRF135 pesticide only. Do not reuse this container for any other purpose. Cleaning the container before final disposal is the responsibility of the person disposing of the container. Cleaning before refilling is the responsibility of the refiller. To clean the container before final disposal, empty the remaining contents from this container into application equipment or mix tank. Fill the container about 10 percent full with water. Agitate vigorously or recirculate water with the pump for 2 minutes. Pour or pump rinsate into application equipment or rinsate collection system. Repeat this rinsing procedure two more times.

LIMITATION OF WARRANTY AND LIABILITY
Read the entire label before using this product, including this Limitation of Warranty and Liability.

If the terms are not acceptable, return the product at once unopened for a refund of the purchase price.

This Company warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes set forth in the Directions for Use, subject to the inherent risks

described below, when used in accordance with the Directions for Use under normal conditions. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, ISAGRO MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY OR ANY OTHER EXPRESS OR IMPLIED WARRANTY.

Buyers and Users of this product must be aware that there are inherent unintended risks associated to the use of this product, independent from the control of Isagro. These risks include, but are not limited to, weather conditions, soil factors, moisture conditions, diseases, irrigation practices, condition of the crop at the time of application, materials which are present in the tank mix with this product or prior to the application of it, cultural practices or the manner of use or application, all risks which are impossible to eliminate. The Buyers and Users should be aware that these factors may cause: ineffectiveness of the product, reduction of harvested yield of the crop (entirely or partially), crop injury or injury to non-target crops or plants or to rotational crops caused by carryover in the soil, resistance of the target weeds to this product. Therefore additional care, treatment and expense are required to take the crop to harvest.

If the Buyer does not agree with the acceptance of these risks, then THE PRODUCT SHOULD NOT BE APPLIED. To the extent consistent with applicable law, by applying this product the Buyer acknowledges and accepts these inherent unintended risks and AGREES THAT ALL SUCH RISKS ASSOCIATED WITH THE APPLICATION AND USE ARE ASSUMED BY THE BUYER.

To the extent consistent with applicable law, ISAGRO or Seller shall not be liable for any incidental, consequential or special damages resulting from the use or handling of this product (including claims based in contract, negligence, strict liability, and other tort or otherwise). To the extent consistent with applicable law, the exclusive remedy of the User or Buyer and the exclusive Liability of Isagro or Seller shall be the return of the purchase price of the product, or at the election of Isagro or Seller, the replacement of the product.

To the extent consistent with applicable law, this Company does not warrant any product reformulated or repackaged from this product except in accordance with this Company's stewardship requirements and with express written permission from this Company.

Isagro or its Seller must have prompt notice of any claim so that an immediate inspection of Buyer's or User's can be made. To the extent consistent with applicable law, if Buyer and User do not notify Isagro or Seller of any claims, in proper time, it shall be barred from obtaining any remedy.

To the extent consistent with applicable law, Buyers and Users are deemed to have accepted the terms of this Limitation of Warranty and Liability, which may not be modified by any verbal or written agreement.

Vegetable and Flower Oils Summary Document
Registration Review: Initial Docket
March 2010
Case 8201

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Approved By:

Keith A. Matthews
Acting Director, Biopesticides and
Pollution Prevention Division

Date: 29 March 2010

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I. PRELIMINARY WORK PLAN

Introduction

The Food Quality Protection Act (FQPA) of 1996 mandated the continuous review of existing pesticides. All pesticides distributed or sold in the United States must generally be registered by EPA, based on scientific data showing that they will not cause unreasonable risks to human health or the environment when used as directed on the product labeling. The registration review program is intended to make sure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the Agency periodically reevaluates pesticides to make sure that as change occurs, products in the marketplace can continue to be used safely. Information on this program is provided at: http://www.epa.gov/oppsrrd1/registration_review/.

The Agency has begun to implement the registration review program pursuant to FIFRA Section 3(g) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration. The Agency will consider benefits information and data as required by FIFRA. The public phase of registration review begins when the initial docket is opened for each case. The docket is the Agency's opportunity to state what it knows about the pesticide and what additional risk analyses and data or information it believes are needed to make a registration review decision. After reviewing and responding to comments and data received in the docket during this comment period, the Agency will develop and commit to a final work plan and schedule for the registration review of Vegetable and Flower Oils.

Vegetable and Flower Oils are oils extracted from leaves, flowers and fruits of plants that exist naturally. These oils are active ingredients in pesticide products registered for use as animal repellents, biochemical pesticides, feeding suppressants, insecticides and miticides. Many of the vegetable and flower oils have other non-pesticidal uses. These uses include food additives, flavorings, and components of cosmetics, soaps, perfumes, plastics, and resins.

The Vegetable and Flower Oils Registration Review Case includes seventeen active ingredients with federally registered products. Currently, there are no Special Local Needs (24c) State Registrations for any of the active ingredients discussed in this case. The Agency issued a Registration Eligibility Document (RED) for Flower and Vegetable Oils in 1993 which included twenty four active ingredients that are categorized as a vegetable and flower oil. For the purposes of registration review, this document covers, as mentioned above, only seventeen active ingredients since the remaining seven active ingredients are considered minimum risk pesticides and are not currently in any federally registered products. The active ingredients covered in this case are:

Oil of Lemongrass, Oil of Eucalyptus, Oil of Mustard, Soybean Oil, Bergamot Oil, Oil of Orange, Alpha-Ionone, Geraniol, Canola Oil, Oil of Citronella, Indole, Castor Oil, Lavandin Oil, Jojoba Oil, Eugenol, Balsam Fir Oil, Oil of Thyme.

The EPA first registered a product containing a Vegetable and Flower Oil active ingredient in 1947. Currently, there are fifty-two end-use products containing these active ingredients that are federally registered as noted above. Forty of the products are for residential use, six for agricultural use and six for both residential and agricultural use. Twenty of the fifty-two products contain only one of these vegetable and flower oils as their active ingredient. The remaining thirty-two products contain additional active ingredients, including pyrethrins, capsaicin, and other vegetable and flower oils.

There are tolerance exemptions established for certain active ingredients included in this registration review case. They are as follows:

§ 180.1127 Biochemical pesticide plant floral volatile attractant compounds: cinnamaldehyde, cinnamyl alcohol, 4-methoxy cinnamaldehyde, 3-phenyl propanol, 4-methoxy phenethyl alcohol, indole, and 1,2,4-trimethoxybenzen reads as follows:

Residues of the biochemical pesticide plant floral volatile attractant compounds: cinnamaldehyde, cinnamyl alcohol, 4-methoxy cinnamaldehyde, 3-phenyl propanol, 4-methoxy phenethyl alcohol, indole, and 1,2,4-trimethoxybenzene are exempt from the requirement of a tolerance in or on the following raw agricultural commodities: the following field crops—alfalfa, clover, cotton, dandelion, peanuts (including hay), rice, sorghum (milo), soybeans, sunflower, sweet potatoes, and wheat; the following vegetable crops—asparagus, beans (including forage hay), beets, carrots, celery, cole crops (cabbage, broccoli, brussels sprouts, cauliflower), collards (kale, mustard greens, turnip greens, kohlrabi), corn, fresh (field, sweet, pop, seed), corn fodder and forage, chinese cabbage, cowpeas, cucurbitis (cucumbers, squash, pumpkin), egg plant, endive (escarole), horseradish (radish, rutabagas, turnip roots), leafy greens (spinach, swiss chard), lettuce (head leaf), okra, parsley, parsnip, peas, peas with pods, peppers, potatoes, sugar beets, tomatoes; the following tree fruit, berry and nut crops—almonds, apples, apricots, berries (blackberry, boysenberry, dewberry, loganberry, raspberry), blueberry, cherry, citrus (grapefruit, kumquat, lemon, lime, orange, tangelo, and tangerine) cranberry, grapes, melons, (watermelon, honeydew, crenshaw, cantaloupe, casaba, persian), nectarines, pears, pecans, peaches, and strawberry as dispersed from the end-use product Corn Rootworm Bait®, a pesticidal bait, in accordance with the prescribed conditions in paragraph (a) of this section.

(a) Cumulative yearly application cannot exceed 20 grams of each floral attractant/acre/application.

(b) [Reserved]

[59 FR 15857, Apr. 5, 1994]

§ 180.1160 Jojoba oil; exemption from the requirement of a tolerance.

The insecticide and spray tank adjuvant jojoba oil is exempted from the requirement of a tolerance in or on all raw agricultural commodities when applied at the rate of 1.0% or less of the final spray in accordance with good agricultural practices, provided the jojoba oil does not contain simmondsin, simmondsin-2-ferulate, and related conjugated organonitriles including demethyl simmondsin and didemethylsimmondsin.

[61 FR 2121, Jan. 25, 1996]

§ 180.1167 Allyl isothiocyanate as a component of food grade oil of mustard; exemption from the requirement of a tolerance.

The insecticide and repellent Allyl isothiocyanate is exempt from the requirement of a tolerance for residues when used as a component of food grade oil of mustard, in or on all raw agricultural commodities, when applied according to approved labeling.

[61 FR 24894, May 17, 1996]

§ 180.1241 Eucalyptus oil; exemption from the requirement of a tolerance.

Time-limited exemptions from the requirement of a tolerance are established for residues of eucalyptus oil on honey and honeycomb in connection with use of the pesticide under section 18 emergency exemptions granted by the EPA. These time-limited exemptions from the requirement of a tolerance for residues of eucalyptus oil will expire and are revoked on June 30, 2007.

[70 FR 37696, June 30, 2005]

§ 180.1251 Geraniol; exemption from the requirement of a tolerance.

An exemption from the requirement of a tolerance is established for residues of the biochemical pesticide geraniol in or on all food commodities.

[69 FR 23151, Apr. 28, 2004]

§ 180.1271 Eucalyptus oil; exemption from the requirement of a tolerance.

An exemption from the requirement of tolerance is established for residues of eucalyptus oil in or on honey, honeycomb, and honeycomb with honey when used at 2g or less eucalyptus oil per hive, where the eucalyptus oil contains 80% or more eucalyptol.

[71 FR 53979, Sept. 13, 2006]

The Agency does not foresee the need for new data or for a new human health risk assessment for these active ingredients. Hazard and exposure information as well as Agency risk assessments on vegetable and flower oils were evaluated against current safety standards established by FIFRA and FFDCA as well as the Agency's scientific

policies and regulations and it was determined that there is no need to conduct an additional human health risk assessment. Vegetable and flower oils are naturally-occurring substances that have non-toxic modes of action (they are primarily repellents) and there is a significant history of exposure to humans and the environment. The Agency believes it is unlikely that any adverse effects would result to the general population from exposure to vegetable and flower oils in the products containing these active ingredients when they are used according to label instructions.

Anticipated Risk Assessment and Data Needs

Human Health Risk Assessment Status

A preliminary human health risk assessment has been conducted as a part of the registration review of vegetable and flower oils. The Agency has determined that based on the available data and information on the vegetable and flower oils, no new data or a new human health risk assessment are expected to be needed at this time for this registration review. Hazard and exposure information as well as the Agency risk assessment on vegetable and flower oils were evaluated against current safety standards as established by statute, regulations, and the Agency's scientific policies. Based on this information, it was determined that there is no need to conduct an additional human health risk assessment. Vegetable and flower oils are naturally-occurring substances that have a non-toxic mode of action and there is a significant history of exposure from these active ingredients to humans and the environment. While there have been reported incidents for seven of the seventeen active ingredients, [see section entitled Incidents, p 30] these reports did not indicate any risk from the use of products that specifically related to the active ingredients. The Agency does not expect any risks associated with these active ingredients when they are used according to the label instructions. Further, these active ingredients are commonly found in foods, and are considered as GRAS substances (Generally Recognized as Safe) by the U.S. FDA. However, should the Agency find that there may be risks associated with any of these active ingredients, they will be further addressed in the Final Work Plan. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist).

Toxicology Data Assessment:

Table 1 Acute Toxicity Profile- Vegetable and Flower Oils						
Active Ingredient (PCC)	**Acute Oral Toxicity Category OPPTS 870.1100**	**Acute Dermal Toxicity Category OPPTS 870.1200**	**Acute Inhalation Toxicity Category OPPTS 870.1300**	**Acute Eye Irritation Category OPPTS 870.2400**	**Acute Dermal Irritation Category OPPTS 870.2500**	**Skin Sensitization Category OPPTS 870.2600**
Oil of mustard (004901)	IV	III	IV	III	IV	**Not a sensitizing Agent
Canola Oil (011332)	IV	IV	IV	IV	IV	**May cause sensitizing
Oil of Citronella (021901)	IV	IV	IV	III	IV	**Not a sensitizing Agent
Indole (025000)	IV	II	Satisfied*	III	IV	Satisfied*
Soybean Oil (031605)	Satisfied*	Satisfied*	Satisfied*	III	Satisfied*	Satisfied*
Castor Oil (031608)	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Lavandin Oil (040500)	Satisfied*	IV	III	Satisfied*	Satisfied*	Satisfied*
Oil of Lemongrass (040502)	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Oil of Eucalyptus (040503)	IV	III	Satisfied*	IV	IV	**Moderate Sensitizing Agent

*A valid scientific rationale regarding the low toxicity of these active ingredients was submitted to the Agency in support of these data requirements.

** (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist).

Active Ingredient (PCC)	Acute Oral Toxicity Category OPPTS 870.1100	Acute Dermal Toxicity Category OPPTS 870.1200	Acute Inhalation Toxicity Category OPPTS 870.1300	Acute Eye Irritation Category OPPTS 870.2400	Acute Dermal Irritation Category OPPTS 870.2500	Skin Sensitization Category OPPTS 870.2600
Oil of Orange (040517)	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Jojoba Oil (067200)	IV	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Eugenol (102701)	III	II	III	Satisfied*	II	**Not a sensitizing Agent
Balsam Fir Oil (129035)	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Bergamot Oil (129029)	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Geraniol (597501)	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Oil of Thyme (597800)	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*	Satisfied*
Alpha-Ionone (129030)	III	III	Satisfied*	Satisfied*	III	Satisfied*

*A valid scientific rationale regarding the low toxicity of these active ingredients was submitted to the Agency in support of these data requirements.

** (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist).

Tier I Biochemical Toxicology Data Requirements were satisfied for all of the active ingredients. No new Tier I biochemical toxicity data are expected to be required for this registration review.

Based on the information presented above, the Agency does not foresee the need for new data or for a new human health risk assessment for this registration review. The Agency believes it is unlikely that any adverse effects would result to the general population from exposure in the use of products containing vegetable and flower oils when they are used according to label instructions.

Environmental Fate and Ecological Risk Assessment Status

The environmental fate data for the vegetable and flower oils have been satisfied due to the low concentration of the active ingredient in end use products, low use volume, and rapid degradation in the environment by normal biological, physical, and /or chemical processes that can be reasonably expected to exist where the pesticides are applied. The Agency does not anticipate the need for additional environmental fate and ecological risk assessments for vegetable and flower oils. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist).

Risk to Threatened and Endangered Species

Based on the lack of toxicity associated with these active ingredients, EPA believes that they will have "No Effect" on any currently listed threatened or endangered species or any designated critical habitat as listed by the U.S. Fish and Wildlife Service (USFWS) and the National Oceanic and Atmospheric Administration's (NOAA) National Marine Fisheries Service (NMFS). EPA anticipates conducting no further analysis of potential risks to endangered or threatened species unless public comments provide additional information that would alter the Agency's current position that Vegetable and Flower Oils will have "No Effect" on such species or their designated habitat. Before making the final determination, the Agency will consider any data or comments submitted during the public comment period.

Product Chemistry

The Agency has conducted a product chemistry assessment of all available data and information associated with vegetable and flower oils as an animal repellent, feeding suppressant, insecticide and miticide in support of this registration review. Based the Agency assessment there is adequate data available on the vegetable and flower oils and therefore the Agency does not foresee the need to require additional generic product chemistry data for this registration review. The data related to the vegetable and flower oils are summarized below:

Oil of mustard (PCC 004901) is listed as an active ingredient in four current registrations with a maximum concentration of 4.43%.

Canola oil (PCC 011332) is listed as an active ingredient in six current registrations with a maximum concentration of 89.5%.

Oil of citronella (PCC 021901) is listed as an active ingredient in thirteen current registrations with a maximum concentration of 4.2%.

Indole (PCC 025000) is listed as an active ingredient in one current registration with a maximum concentration of 0.2%.

Soybean oil (PCC 031605) is listed as an active ingredient in three current registrations with a maximum concentration of 98%.

Castor oil (PCC 031608) is listed as an active ingredient in one current registration with a maximum concentration of 100%.

Lavandin oil (PCC 040500) is listed as an active ingredient in two current registrations with a maximum concentration of 17.29%.

Oil of lemongrass (PCC 040502) is listed as an active ingredient in two current registrations with a maximum concentration of 2%.

Oil of eucalyptus (PCC 040503) is listed as an active ingredient in six current registrations with a maximum concentration of 100%.

Oil of orange (PCC 040517) is listed as an active ingredient in two current registrations with a maximum concentration of 0.02%.

Jojoba oil (PCC 067200) is listed as an active ingredient in two current registrations with a maximum concentration of 97.5%.

Eugenol (PCC 102701) is listed as an active ingredient in thirteen current registrations with a maximum concentration of 4.2%.

Balsam Fir Oil (PCC 129035) is listed as an active ingredient in two current registrations with a maximum concentration of 10%.

Bergamot oil (PCC 129029) is listed as an active ingredient in two current registrations with a maximum concentration of 0.11%.

Geraniol (PCC 597501) is listed as an active ingredient in eleven current registrations with a maximum concentration of 17.28%.

Oil of thyme (PCC 597800) is listed as an active ingredient in one current registration with a maximum concentration of 36%.

Alpha-Ionone (PCC 129030) is listed as an active ingredient in two current registrations with a maximum concentration of 0.01%.

Physical and Chemical Characteristics

The product chemistry database for Vegetable and Flower Oils is complete and adequately fulfills the guideline data requirements. There are no reported impurities of toxicological concern. The data related to the vegetable and flower oils are summarized below:

Oil of Mustard	
Common name	Oil of Mustard
CAS Registry Number	57-06-7
End-use products/EP	Outdoor Animal Repellent (0.216% AI); Insect control Concentrate (4.43% AI); Scent-OFF Aroma Pouches (0.2% AI); Scent-Off Pellets (0.2% AI).

Physical and Chemical Properties for Oil of Mustard		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Colorless
830.6303	Physical state	Liquid at ambient temp
830.6304	Odor	Pungent
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	N/A
830.7220	Boiling point/boiling range	152 °C
830.7300	Density	1.02 g/mL at 15°C
830.7520	Particle size, fiber length, and diameter distribution	N/A
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		N/A
830.7840	Water solubility	slightly soluble, miscible whether, chloroform, and benzene
830.7950	Vapor pressure	3.5 mmHg

Canola Oil	
Common name	Canola Oil
CAS Registry Number	120962-03-0
End-use products/EP	NEU 1160 Vegetable Oil Insecticide (96% AI); NEU1161 (89.5% AI); NEU1161 RTU (1% AI); NEU1161 Residual Pest Spray (1% AI); Aerosol NEU1161 Residual Pest Spray (1% AI); Aerosol NEU1161 RTU (0.01% AI)

Physical and Chemical Properties for Canola Oil

Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	pale yellow
830.6303	Physical state	liquid
830.6304	Odor	odorless
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	6.82
830.7220	Boiling point/boiling range	N/A
830.7300	Density	0.92 g/mL at 19.5°C
830.7520	Particle size, fiber length, and diameter distribution	N/A
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		EP testing
830.7840	Water solubility	soluble
830.7950	Vapor pressure	EP testing

Oil of Citronella	
Common name	Oil of Citronella
CAS Registry Number	8000-29-1
End-use products/EP	Cutter Insect Repellent RDCO31RN (3% AI); Cutter Insect Repellent ICARUS (3% AI); Cutter Repellent PROMETHCUS (3% AI); TPC EQUI_SPRAY "N" WIPE (1% AI); Bug Block Sunscreen & Insect Repellent (4.2% AI); OFF! Citronella Candle (3% AI); Fiebing's Fly spray 44 (1% AI); Buzz away insect repellent (5% AI); Buzz Away insect repellent towlettes (5% AI); Aloe herbal horse spray (0.75% AI); Aloe Herbal horse spray ready-to-use (0.15%AI); Scent –Off aroma pouches (1.2%AI); Scent-Off pellets (1.2%AI).

Physical and Chemical Properties for Oil of Citronella		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Not Required
830.6303	Physical state	Not Required
830.6304	Odor	Not Required
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Not Required
830.7000	pH	Not Required
830.7220	Boiling point/boiling range	Not Required
830.7300	Density	Not Required
830.7520	Particle size, fiber length, and diameter distribution	Not Required
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		Not Required
830.7840	Water solubility	Not Required
830.7950	Vapor pressure	Not Required

Indole	
Common name	Indole
CAS Registry Number	120-7-9
End-use products/EP	Bull Run Fly Attractant (0.2% AI).

Physical and Chemical Properties for Indole		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	White
830.6303	Physical state	Solid
830.6304	Odor	Fecal odor
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	5.9 at 25°C
830.7220	Boiling point/boiling range	52.5°C (melting range)
830.7300	Density	1.22 g/mL
830.7520	Particle size, fiber length, and diameter distribution	N/A
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		log Kow =2.14
830.7840	Water solubility	3.56 g/mL
830.7950	Vapor pressure	0.0122 mmHg

Soybean Oil	
Common name	Soybean Oil
CAS Registry Number	8001-22-7
End-use products/EP	Citru-Soy (98% AI); Drexel Soydorm oil (98% AI); Golden Pest Spray Oil (93% AI).

Physical and Chemical Properties for Soybean Oil		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Amber
830.6303	Physical state	Liquid
830.6304	Odor	Slightly aromatic
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	7.5
830.7220	Boiling point/boiling range	>250oC
830.7300	Density	7.68 lbs/gal @20oC
830.7520	Particle size, fiber length, and diameter distribution	N/A
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		N/A
830.7840	Water solubility	Emulsifies upon contact with water
830.7950	Vapor pressure	N/A

Castor oil	
Common name	Castor Oil
CAS Registry Number	8001-79-4
End-use products/EP	Scoot Mole Evacuator (100% AI).

Physical and Chemical Properties for Castor Oil		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Not Required
830.6303	Physical state	Not Required
830.6304	Odor	Not Required
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Not Required
830.7000	pH	Not Required
830.7220	Boiling point/boiling range	Not Required
830.7300	Density	Not Required
830.7520	Particle size, fiber length, and diameter distribution	Not Required
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		Not Required
830.7840	Water solubility	Not Required
830.7950	Vapor pressure	Not Required

Lavandin Oil	
Common name	Lavandin Oil
CAS Registry Number	8022-15-9
End-use products/EP	OFF! Moth Proofer 5 (11.49% AI); Recede (17.29% AI).

Physical and Chemical Properties for Oil of Mustard		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	White
830.6303	Physical state	Liquid
830.6304	Odor	Odorless
830.6313	Stability to normal and elevated temperatures, metals and metal ions	N/A
830.7000	pH	8.4 at 25°C
830.7220	Boiling point/boiling range	N/A
830.7300	Density	N/A
830.7520	Particle size, fiber length, and diameter distribution	N/A
830.7550	Partition coefficient (n-Octanol/Water)	N/A
830.7560		N/A
830.7570		N/A
830.7840	Water solubility	N/A
830.7950	Vapor pressure	N/A

Oil of Lemomgrass	
Common name	Oil of Lemoongrass
CAS Registry Number	8007-02-1
End-use products/EP	Scent-Off Aroma Pouches (2% AI); Scent-OFF Pellets (2% AI).

Physical and Chemical Properties for Oil of Lemongrass

Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	pale yellow
830.6303	Physical state	liquid
830.6304	Odor	herbaceous odor
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	N/A
830.7220	Boiling point/boiling range	N/A
830.7300	Density	0.855 g/mL
830.7520	Particle size, fiber length, and diameter distribution	N/A
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		N/A
830.7840	Water solubility	N/A
830.7950	Vapor pressure	N/A

Oil of Eucalyptus	
Common name	Oil of Eucalyptus
CAS Registry Number	8000-48-4
End-use products/EP	Repel essential insect repellent lotion (30% AI); Repel essential insect repellent pump spray (40% AI); Citriodiol (100% AI); Repellent insect repellent 30 LE (30% AI); API Life VAR (16% AI); Mint-X trash bags (0.04% AI).

Physical and Chemical Properties for Oil of Eucalyptus

Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	EP Testing
830.6303	Physical state	EP Testing
830.6304	Odor	EP Testing
830.6313	Stability to normal and elevated temperatures, metals and metal ions	EP Testing
830.7000	pH	EP Testing
830.7220	Boiling point/boiling range	EP Testing
830.7300	Density	EP Testing
830.7520	Particle size, fiber length, and diameter distribution	EP Testing
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		EP Testing
830.7840	Water solubility	EP Testing
830.7950	Vapor pressure	EP Testing

Oil of Orange	
Common name	Oil of Orange
CAS Registry Number	8008-57-9
End-use products/EP	Scent-Off Aroma Pouches (0.02% AI); Scent-OFF Pellets (0.02% AI).

Physical and Chemical Properties for Oil of Orange		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	EP Testing
830.6303	Physical state	EP Testing
830.6304	Odor	EP Testing
830.6313	Stability to normal and elevated temperatures, metals and metal ions	EP Testing
830.7000	pH	EP Testing
830.7220	Boiling point/boiling range	EP Testing
830.7300	Density	EP Testing
830.7520	Particle size, fiber length, and diameter distribution	EP Testing
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		EP Testing
830.7840	Water solubility	EP Testing
830.7950	Vapor pressure	EP Testing

Jojoba Oil	
Common name	Jojoba Oil
CAS Registry Number	61789-91-1
End-use products/EP	Detur (97.5% AI); E-Rase ready to –use (0.5% AI).

Physical and Chemical Properties for Jojoba Oil		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	EP Testing
830.1200	Description of starting materials, production and formulation process	EP Testing
830.1400	Discussion of formation of impurities	EP Testing
830.1700	Preliminary Analysis	EP Testing
830.6302	Color	EP Testing
830.6303	Physical state	EP Testing
830.6304	Odor	EP Testing
830.6313	Stability to normal and elevated temperatures, metals and metal ions	EP Testing
830.7000	pH	EP Testing
830.7220	Boiling point/boiling range	EP Testing
830.7300	Density	EP Testing
830.7520	Particle size, fiber length, and diameter distribution	EP Testing
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		EP Testing
830.7840	Water solubility	EP Testing
830.7950	Vapor pressure	EP Testing

Eugenol	
Common name	Eugenol
CAS Number	97-53-0
End-use products/EP	Raid EO ARK (0.5% AI); Lure N Kill Japanese Beetle (23% AI); Bag-A-Bug Japanese Beetle Trap (23% AI); Japanese Beetle (21.98% AI); Japanese Beetle Bait II (22.25% AI); Trece Japanese Beetle Trap (22.25% AI); Surefire Japanese beetle trap (25.233% AI); Ecopco Jet Contact Insecticide (2.5% AI); Ecozap Wasp & Hornet Insecticide (0.05% AI); Ecozap Crawling and flying insecticide (0.05% AI); Bull Run Japanese & Oriental Beetle Trap (15.48% AI).

Physical and Chemical Properties for Eugenol		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Pale to dark yellow
830.6303	Physical state	Liquid
830.6304	Odor	Sweet spicy clove woody
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	6.8 at 21°C
830.7220	Boiling point/boiling range	264.2°C
830.7300	Density	1.050 g/mL
830.7520	Particle size, fiber length, and diameter distribution	Not found?
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		2.73
830.7840	Water solubility	Insoluble
830.7950	Vapor pressure	0.00948 mmHg

Balsam Fir Oil	
Common name	Balsam Fir Oil
CAS Registry Number	8021-28-1
End-use products/EP	Fresh Cab (2% AI); Canadian Wilderness Oil (10% AI).

Physical and Chemical Properties for Balsam Fir Oil		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	EP Testing
830.1200	Description of starting materials, production and formulation process	EP Testing
830.1400	Discussion of formation of impurities	EP Testing
830.1700	Preliminary Analysis	EP Testing
830.6302	Color	EP Testing
830.6303	Physical state	EP Testing
830.6304	Odor	EP Testing
830.6313	Stability to normal and elevated temperatures, metals and metal ions	EP Testing
830.7000	pH	EP Testing
830.7220	Boiling point/boiling range	EP Testing
830.7300	Density	EP Testing
830.7520	Particle size, fiber length, and diameter distribution	EP Testing
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		EP Testing
830.7840	Water solubility	EP Testing
830.7950	Vapor pressure	EP Testing

Bergamot Oil	
Common name	Bergamot Oil
CAS Registry Number	8007-75-8
End-use products/EP	Scent-Off Aroma Pouches (0.11% AI); Scent-OFF Pellets (0.11% AI).

Physical and Chemical Properties for Bergamot Oil		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	EP Testing
830.6303	Physical state	EP Testing
830.6304	Odor	EP Testing
830.6313	Stability to normal and elevated temperatures, metals and metal ions	EP Testing
830.7000	pH	EP Testing
830.7220	Boiling point/boiling range	EP Testing
830.7300	Density	EP Testing
830.7520	Particle size, fiber length, and diameter distribution	EP Testing
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		EP Testing
830.7840	Water solubility	EP Testing
830.7950	Vapor pressure	EP Testing

Geraniol	
Common name	Geraniol
CAS Registry Number	106-24-1
End-use products/EP	Lure N Kill Japanese beetle (9.84% AI); Bag-A-Bug Japanese Beetle Trap (2.84% AI); Japanese Beetle combo bait (9.43% AI); Japanese Beetle Bait II (9.5% AI); Trece Japanese beetle trap (9.5% AI); Surefire Japanese beetle trap (10.698% AI); Shooter insecticide (17.28% AI); Biomite (0.417% AI); Scent-OFF Aroma pouches (0.04% AI); Scent-OFF Pellets (0.04% AI); Bull Run Japanese & oriental beetle trap (6.622% AI).

Physical and Chemical Properties for Geraniol		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Colorless
830.6303	Physical state	Liquid
830.6304	Odor	sweet floral fruity rose waxy
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	6.3 at 20°C
830.7220	Boiling point/boiling range	239.89oC
830.7300	Density	7.231 lbs/gal
830.7520	Particle size, fiber length, and diameter distribution	Not found?
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		3.47
830.7840	Water solubility	insoluble
830.7950	Vapor pressure	0.0159 mmHg

Oil of Thyme	
Common name	Oil of Thyme
CAS Registry Number	8007-46-3
End-use products/EP	Shooter Insecticide (36% AI).

Physical and Chemical Properties for Oil of Thyme		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Not Required
830.6303	Physical state	Not Required
830.6304	Odor	Not Required
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Not Required
830.7000	pH	Not Required
830.7220	Boiling point/boiling range	Not Required
830.7300	Density	Not Required
830.7520	Particle size, fiber length, and diameter distribution	Not Required
830.7550	Partition coefficient (n-Octanol/Water)	Not Required
830.7560		Not Required
830.7570		Not Required
830.7840	Water solubility	Not Required
830.7950	Vapor pressure	Not Required

Alpha-Ionone	
Common name	Alpha-Ionone
CAS Registry Number	127-41-3
End-use products/EP	Scent-Off Aroma Pouches (0.01% AI).

Physical and Chemical Properties for Alpha-Ionone		
Guideline Reference No.	Property	Description of Result
830.1100	Product identity and composition	CBI
830.1200	Description of starting materials, production and formulation process	CBI
830.1400	Discussion of formation of impurities	CBI
830.1700	Preliminary Analysis	CBI
830.6302	Color	Pale yellow
830.6303	Physical state	Liquid
830.6304	Odor	Cedar wood
830.6313	Stability to normal and elevated temperatures, metals and metal ions	Stable
830.7000	pH	N/A
830.7220	Boiling point/boiling range	238°C
830.7300	Density	0.931 g/mL
830.7520	Particle size, fiber length, and diameter distribution	N/A
830.7550	Partition coefficient (n-Octanol/Water)	EP Testing
830.7560		EP Testing
830.7570		N/A
830.7840	Water solubility	N/A
830.7950	Vapor pressure	<1 mmHg at 68°C

Incidents

Products containing seven of the active ingredients had reported incidents. They are: Oil of Mustard, Canola Oil, Oil of Citronella, Eugenol, Geraniol, Lavandin Oil, and Oil of Eucalyptus. The incidents reported for four of the seven active ingredients (Oil of Mustard, Canola Oil, Eugenol, and Geraniol) contained additional active ingredients. The Agency believes that the presence of these other active ingredients is likely to increase the overall toxicity of the product. A review of the details from each incident report prompted the Agency to look for trends that may indicate any threat to human health. Several incidents that were reported point to product misuse and the symptoms reported were attributable to the presence of the other active ingredient(s) in the product. These reports did not indicate any risk from the use of products that specifically related to the active ingredients. The Agency does not expect any risks associated with these active ingredients when they are used according to the label instructions. Further, these active ingredients are commonly found in foods, and are considered as GRAS substances (Generally Recognized as Safe) by the U.S. FDA. However, should the Agency find that there may be risks associated with any of these active ingredients, they will be further addressed in the Final Work Plan. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist).

Endocrine Disruptor Screening Program

As required under FFDCA section 408(p), EPA has developed the Endocrine Disruptor Screening Program (EDSP) to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier I testing consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier I screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier II tests are necessary based on the available data. Tier II testing is designed to identify any adverse endocrine related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. This list of chemicals was selected based on the potential for human exposure through pathways such as food and water, residential activity, and certain post-application agricultural scenarios. This list should not be construed as a list of known or likely endocrine disruptors.

Vegetable and Flower Oils are not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Under FFDCA sec. 408(p) the Agency must screen all pesticide chemicals. Accordingly, EPA anticipates issuing future EDSP test orders/data call-ins for all pesticide active ingredients.

For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, the test guidelines and the Tier I screening battery, please visit our website: http://www.epa.gov/endo/.

Timeline

EPA has created the following estimated timeline for the completion of the Vegetable and Flower Oils registration review:

Table 4 Estimated Timeline

Activities	Estimated Month/Year
Phase 1: Opening the docket	
Open Public Comment Period for Vegetable and Flower Oils Docket	March 2010
Close Public Comment Period	May 2010
Phase 2: Case Development	
Develop Final Work Plan (FWP)	September 2010
Phase 3: Registration Review Decision	
Open Public Comment Period for Proposed Reg. Review Decision	March 2011
Close Public Comment Period	May 2011
Final Decision and Begin Post-Decision Follow-up	June 2011
Estimated Total (years)	1 year, 3 months

Guidance for Commenters

The public is invited to comment on EPA's preliminary registration review work plan and rationale. The Agency will consider all comments as well as any additional information or data provided in a timely manner prior to issuing a final work plan for the Vegetable and Flower Oils case.

Environmental Justice

EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical, unusually high exposure to Vegetable and Flower Oils, compared to the general population. Please comment if

you are aware of any sub-populations that may have atypical, unusually high exposure compared to the general population.

Water Quality

Vegetable and Flower Oils are not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885. In addition, no Total Maximum Daily Loads (TMDL) have been developed for [insert pesticide], based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES. More information on impaired water bodies and TMDLs can be found at http://www.epa.gov/owow/tmdl/. The Agency invites submission of water quality data for this pesticide. To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process* (see: http://www.epa.gov/oppsrrd1/registration_review/water_quality_sop.htm) in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

Trade Irritants

Through the registration review process, the Agency intends to solicit information on trade irritants and, to the extent feasible, take steps toward facilitating irritant resolution. Growers and other stakeholders are asked to comment on any trade irritant issues resulting from lack of Maximum Residue Limits (MRLs) or disparities between U.S. tolerances and MRLs in key export markets, providing as much specificity as possible regarding the nature of the concern. Given the fact that active ingredients in this case are supported by tolerance exemptions, no MRL's would be expected to be established. Therefore, the Agency does not anticipate current uses of Vegetable and Flower Oils posing concerns as a trade irritant.

Additional Information

Stakeholders are also specifically asked to provide available information and data in the following areas:

1. Confirmation on the following label information:
    a. Sites of application
    b. Formulations
    c. Application methods and equipment
    d. Maximum application rates
    e. Frequency of application, application intervals and maximum number of applications
    f. Geographic limitations on use

2. Use or potential use distribution
3. Use history
4. Usage/use information for non-agricultural uses (e.g., materials preservation)
5. Typical application interval
6. State or local use restrictions
7. Monitoring data

Next Steps

After the 60-day comment period closes, the Agency will review and respond to any comments received in a timely manner and then issue a Final Work Plan for the Vegetable and Flower Oils Case.

II. FACT SHEET

A. Canola Oil

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Canola Oil PC Code: 011332
- Canola Oil:
  - CAS#: 120962-03-0

  Other Chemical Names: N/A
- Technical registrants: N/A (Registrant for EP with highest AI concentration: W. NEUDORFF GMBH KG)
- First approved for use in a registered product as a biochemical classified insecticide/miticide in 1998.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Canola Oil is an edible refined vegetable oil obtained from the seeds of four species of rape plants, Brassica napus, Brassica juncea, Brassica Rapa and B. campestris of the family Cruciferee (mustard family). Canola oil is considered safe for human consumption. Canola Oil repels insects by altering the outer layer of the leaf surface or by acting as an insect irritant.

Use Information

- Use Sites: Canola Oil is registered for use on a wide range of plants, including: citrus, corn, fruit trees, nut trees, sugar beets, soybeans, tomatoes, vegetable figs, melon, olives, small fruits, alfalfa, bedding plants, ornamentals and houseplants.
- Target pest: mites, whiteflies, flies, spider, gnats, insects (eggs)

- Application Methods: The products are applied either with spray or irrigation systems.
- There are currently six biochemical pesticide registrations.

Recent Actions

There have been no recent significant regulatory activities regarding Canola Oil products (i.e., tolerance related actions, changes of use patterns, submission of toxicological studies).

Human Health Risk Assessment

Canola Oil was first registered in 1998 as a biochemical insecticide. The Agency does not foresee the need for new data or for a new human health risk assessment for Canola Oil for this registration review. It is a naturally-occurring substance that has a non-toxic mode of action. There have been reported incidents for Canola Oil. See Incident section on page 30 of this document. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Canola Oil have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Canola Oil is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
67702-4	NEU 1160 VEGETABLE OIL INSECTICIDE	67702	W. NEUDORFF GMBH KG
67702-5	NEU1161	67702	W. NEUDORFF GMBH KG
67702-6	NEU1161 RTU	67702	W. NEUDORFF GMBH KG
67702-14	NEU1161 RESIDUAL PEST SPRAY	67702	W. NEUDORFF GMBH KG
67702-16	AEROSOL NEU1161 RESIDUAL PEST SPRAY	67702	W. NEUDORFF GMBH KG
67702-20	AEROSOL NEU1161 RTU	67702	W. NEUDORFF GMBH KG

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home

B. Oil of Mustard

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Oil of Mustard PC Code: 004901
- Oil of Mustard:
  - CAS#: 57-06-7

  Other Chemical Names: 1-Propene, 3-isothiocyanato-
  2-Propenyl isothiocyanate
  3-Isothiocyanato-1-propene
  Allyl isosulfocyanate
  Allyl isothiocyanate
  Allyl mustard oil

- Technical registrants: N/A (Registrant for EP with highest AI concentration: CHAMPON MILLENNIUM CHEMICALS, INC.)
- First approved for use in a registered product as a biochemical classified insecticide in 1962.
- Biopesticide and Pollution Prevention Registration Review Lead:

Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Oil of Mustard is an active ingredient in four pesticide products that are registered for use as an insect and animal repellent and feeding suppressant. Oil of Mustard is isolated from the black mustard seed, Brassica Ingra L. (Family: Cruciferae). It may also be prepared from allyl iodide and potassium thiocyanate. It is colorless to pale yellow liquid. Oil of Mustard is slightly soluble in water and miscible with alcohol and most organic solvents. The Allyl moiety, which is a component of numerous odoriferous compounds, probably contributes to the odor of the compound which forms the basis of its repellent action toward insects and animals.

Use Information

- Use Sites: Household/domestic dwellings contents, household domestic dwellings indoor premises, ornamental and/or shade trees, ornamental lawns and turf, ornamental woody shrubs and vines, farm or agricultural structures/premises, bird feeding areas and refuse and solid waste containers.
- Target pest: centipedes, millipedes, spiders, earwigs, silverfish, ants, cockroaches, water bugs, crickets, squirrels, dog, raccoon, cats, and deer.
- Application Methods: aerosol can, sprayer, by hand, and trigger spray bottle.
- There are four biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED) was issued in December 1993 for Flower and Vegetable Oils which included Oil of Mustard.

Human Health Risk Assessment

Oil of Mustard was first registered in 1962 as a biochemical pesticide. The Agency does not foresee the need for new data or for a new human health risk assessment for Oil of Mustard for this registration review. Oil of Mustard is included in the Vegetable and Flower Oils case. It is a naturally-occurring substance that has a non-toxic mode of action. There have been reported incidents for Oil of Mustard. See Incident section on page 30 of this document. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Oil of Mustard have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical,

and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Oil of Mustard is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from the use of this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
50932-9	OUTDOOR ANIMAL REPELLENT	50932	WOODSTREAM CORPORATION
61966-4	INSECT CONTROL CONCENTRATE	61966	CHAMPON MILLENNIUM CHEMICALS, INC.
74693-1	SCENT-OFF AROMA POUCHES	74693	BAKER'S & 18 CORPORATION
74693-2	SCENT-OFF PELLETS	74693	BAKER'S & 18 CORPORATION

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

C. Oil of Citronella

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Oil of Citronella PC Code: 021901
- Oil of Citronella:
  - CAS#: 8000-29-1

  Other Chemical Names: N/A

- Technical registrants: N/A (Registrant for EP with highest AI concentration: QUANTUM INC)
- First approved for use in a registered product as a biochemical classified insecticide/repellent in 1984.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Oil of Citronella is an active ingredient in products registered for use as an insect and animal repellent. Oil of Citronella is volatile, liquid oil derived from dried cultivated grasses. It has a distinctive odor which may make it difficult for some pests to locate a host. The length of repellency time varies with the inert ingredient and amount of oil of citronella in product.

Use Information

- Use Sites: Oil of Citronella is registered for use on humans to repel insects. It is registered for use in recreational areas, outdoor household areas, and around trees and shrubs.
- Target pest: Various specific insects including mosquitos, black flies, fleas and ticks.
- Application Methods: The products are applied in various ways. Liquid products are sprayed or applied by hand (cloth wipe-on) on skin or clothing. As a solid, it is used as candles, cartridges, and rub-on products.
- There are currently thirteen biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED), Case 3105 was issued for Oil of Citronella.

Human Health Risk Assessment

Oil of Citronella was first registered in 1948 as a biochemical pesticide. Oil of Citronella is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There have been reported incidents for Oil of Citronella. See Incident section on page 30 of this document. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Oil of Citronella have been satisfied due to the low concentration of the active ingredient in the end use products, low

use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Oil of Citronella is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
121-79	CUTTER INSECT REPELLENT RDCO31RN	121	SPECTRUM, A DIV OF UNITED INDUSTRIES CORP
121-80	CUTTER INSECT REPELLENT ICARUS	121	SPECTRUM, A DIV OF UNITED INDUSTRIES CORP
121-85	CUTTER INSECT REPELLENT PROMETHCUS	121	SPECTRUM, A DIV OF UNITED INDUSTRIES CORP
270-274	TPC EQUI-SPRAY "N" WIPE	270	FARNAM COMPANIES, INC.
1543-14	BUG BLOCK SUNSCREEN & INSECT REPELLENT	1543	W.F. YOUNG, INC.
4822-422	OFF! CITRONELLA CANDLE	4822	S.C. JOHNSON & SON INC.
9816-2	FIEBING'S FLYSPRAY 44	9816	FIEBING COMPANY, INC.
66551-4	BUZZ AWAY INSECT REPELLENT	66551	QUANTUM INC
66551-6	BUZZ AWAY INSECT REPELLENT TOWELETTES	66551	QUANTUM INC

66963-8	ALOE HERBAL HORSE SPRAY	66963	ESPREE ANIMAL PRODUCTS, INC
66963-9	ALOE HERBAL HORSE SPRAY READY-TO-USE	66963	ESPREE ANIMAL PRODUCTS, INC
74693-1	SCENT-OFF AROMA POUCHES	74693	BAKER'S & 18 CORPORATION
74693-2	SCENT-OFF PELLETS	74693	BAKER'S & 18 CORPORATION

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

D. Indole

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Indole PC Code: 025000
- Indole:
  - CAS#: 120-72-9

  Other Chemical Names: 1- Azaindene
  1- Benzazole
  1- Benzo(b)pyrrole
  2,3- Benzopyrole
  2,3- Benzopyrrole
  Indole
  Ketone
- Technical registrants: N/A (Registrant for EP with highest AI concentration: QU BULL RUN SCIENTIFIC, VBT)
- First approved for use in a registered product as a biochemical classified insecticide/ attractant in 1994.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Indole is a naturally-occurring, aromatic substance that is responsible for the fecal odors associated with human waste. As all animal waste contains indole, as do some plants and other naturally-occurring substances, it is ubiquitous in the environment. At high concentrations, it gives off the odor of feces but at lower concentrations, it smells flowery. For this reason, it is a common ingredient in perfumes and synthetically-

produced essential oils, such as jasmine oil. Indole is also a major constituent of coal tar, the main industrial source, but was first isolated from indigo for use as a dyestuff.

Use Information

- Use Sites: Indole is an active ingredient in products registered for use to attract and trap filth flies. It is registered for use outdoors.
- Target pest: Filth flies
- Application Methods: The product is an attractant pouch that is placed in a fly trap.
- There is currently one biochemical pesticide registration.

Recent Actions

A Biopesticides Registration Action Document (BRAD) was issued in May 2009 for Indole.

Human Health Risk Assessment

Indole was first registered in 1994 as a biochemical pesticide. Indole is a naturally-occurring substance that has a non-toxic mode of action and has a significant history of exposure to humans and the environment. There are no incident reports on file with the Agency for Indole.(February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Indole have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Indole is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
84565-2	BULL RUN FLY ATTRACTANT	84565	BULL RUN SCIENTIFIC, VBT

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

E. Soybean Oil

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Soybean Oil PC Code: 031605
- Soybean Oil:
  - CAS#: 8001-22-7

  Other Chemical Names: N/A
- Technical registrants: N/A (Registrant for EP with highest AI concentration: DREXEL CHEMICAL COMPANY)
- First approved for use in a registered product as a biochemical classified insecticide in 1959.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Soybean Oil is a complex mixture of substances that come from various parts of the plants such as flowers, fruits, and wood. Soybean Oil is obtained from soybeans, glycine max., by solvent extraction using petroleum hydrocarbons or, to a lesser extent, by expression using continuous screw press operations. The oil is usually refined with alkali. Soybean Oil is a pale yellow to brownish yellow oil. It is miscible with organic solvents. Soybean is also considered to be GRAS by FDA (21 CFR 173.340 and 182.70) and is commonly used as a human food additive.

Use Information

- Use Sites: Soybean Oil is an active ingredient in products registered for use on food and feed crops, ornamental plants. It is registered for use indoor and outdoors.
- Target pest: Mites, beetles and other insects.

- Application Methods: The product is applied by sprayer, ground or aerial applications.
- There are currently three biochemical pesticide registrations.

Recent Actions

There have been no recent significant regulatory activities regarding Soybean Oil (i.e., tolerance related actions, changes of use patterns, submission of toxicological studies or incident reports.)

Human Health Risk Assessment

Soybean Oil was first registered in 1959 as a biochemical pesticide. Soybean Oil is a naturally-occurring substance that has a non-toxic mode of action and has a significant history of exposure to humans and the environment. There are no incident reports on file with the Agency for Soybean Oil. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Soybean Oil have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Soybean Oil is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
19713-603	CITRU-SOY	19713	DREXEL CHEMICAL COMPANY
19713-605	DREXEL SOYDORM OIL	19713	DREXEL CHEMICAL COMPANY
57538-11	GOLDEN PEST SPRAY OIL	57538	STOLLER ENTERPRISES, INC

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

F. Castor Oil

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Castor Oil PC Code: 031608
- Castor Oil:
  - CAS#: 8001-79-4

  Other Chemical Names: Ricinus Oil
- Technical registrants: BALK FAMILY TRUST
- First approved for use in a registered product as a biochemical classified insecticide/miticide in 1994.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Castor Oil is a vegetable oil obtained from the castor bean (technically castor seed as the castor plant, Ricinus communis, is not a member of the bean family). Castor Oil is colorless to very pale yellow liquid with mild or no odor or taste. It is a triglyceride in which approximately ninety percent of fatty acid chains are ricinoleic acid. Oleic and linoleic acids are the other significant compounds.

Use Information

- Use Sites: Castor Oil is an active ingredient in products registered for use as mold inhibitors.
- Target pest: Mole, Voles, Gophers from lawns, ornamentals, turf, golf courses and athletic fields.

- Application Methods: The product is applied with sprayer.
- There is currently one biochemical pesticide registration.

Recent Actions

There have been no recent significant regulatory activities regarding Castor Oil (i.e., tolerance related actions, changes of use patterns, submission of toxicological studies or incident reports.)

Human Health Risk Assessment

Castor Oil was first registered in 1994 as a biochemical pesticide. Castor Oil is a naturally-occurring substance that has a non-toxic mode of action. There are no incident reports on file with the Agency for Castor Oil. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Castor Oil have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Castor Oil is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
65615-1	SCOOT MOLE EVACUATOR	65615	BALK FAMILY TRUST

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

G. Lavandin Oil

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Lavandin Oil PC Code: 040500
- Lavandin Oil:
  - CAS#: 8022-15-9

  Other Chemical Names: N/A
- Technical registrants: N/A (Registrant for EP with highest AI concentration: S.C. JOHNSON & SON INC.)
- First approved for use in a registered product as a biochemical classified insecticide/miticide in 1996.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Lavandin Oil is plant oil which includes complex mixtures of natural components of plants, such as flowers, fruits, and wood. They are responsible for the distinctive odor or flavor of the plant they come from. Lavandin Oil is an active ingredient in products registered for use as an insect repellent.

Use Information

- Use Sites: Lavandin Oil is an active ingredient in products registered for use in homes, especially closets, drawers, clothes storage containers.
- Target pest: moth
- Application Methods: The products are applied as a cartridge.
- There are currently two biochemical pesticide registration

Recent Actions

There have been no recent significant regulatory activities regarding Lavandin Oil (i.e., tolerance related actions, changes of use patterns, submission of toxicological studies or incident reports.)

Human Health Risk Assessment

Lavandin Oil was first registered in 1996 as a biochemical pesticide. It is a naturally-occurring substance that has a non-toxic mode of action. There have been

reported incidents for Lavandin Oil. See Incident section on page 30 of this document. February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Lavandin Oil have been satisfied due to the low concentration in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target waiver requests were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Lavandin Oil is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. The Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by waivers due to low toxicity and exposure use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
4822-440	OFF! MOTH PROOFER 5	4822	S.C. JOHNSON & SON INC.
4822-485	RECEDE 14490P163	4822	S.C. JOHNSON & SON INC.

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

H. Oil of Lemongrass

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Oil of Lemongrass PC Code: 040502

- Oil of Lemongrass:
  - CAS#: 8007-02-1

  Other Chemical Names: N/A
- Technical registrants: N/A (Registrant for EP with highest AI concentration: BAKER'S & 18 Corporation)
- First approved for use in a registered product as a biochemical classified insecticide/ repellent in 1962.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Oil of Lemongrass is a volatile oil expressed from grasses Cymbopogon Andropogon citratus or Cymbopogon flexuosus. It is used as a source of citral which in turn is used in the synthesis of vitamin A. Oil of Lemongrass is a reddish-yellow or brownish-red liquid. It has a strong odor of verbena. It is slightly soluble in water and soluble in alcohol, chloroform and ether. It is composed mostly (75-85%) of citral, methylheptenone, citronellal, geraniol, limonene, and dipentane. Oil of Lemongrass, is commonly used in food flavoring and cosmetics and is listed by FDA as GRAS (21 CFR 182.20).

Use Information

- Use Sites: Oil of Lemongrass is an active ingredient in products registered for use on ornamental herbaceous plants, ornamental woody shrubs and vines, ornamental and shade to repel dogs and cats.
- Target pest: Dogs and cats
- Application Methods: The products are applied with an aroma pouch and sprinkled by hand with pellets.
- There are currently two biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED) was issued in December 1993 for Flower and Vegetable Oils which included Oil of Lemongrass.

Human Health Risk Assessment

Oil of Lemongrass was first registered in 1962 as a biochemical pesticide. It is a naturally-occurring substance that has a non-toxic mode of action. There are no incident reports on file with the Agency for Oil of Lemongrass. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Oil of Lemongrass have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Oil of Lemongrass is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
74693-1	SCENT-OFF AROMA POUCHES	74693	BAKER'S & 18 CORPORATION
74693-2	SCENT-OFF PELLETS	74693	BAKER'S & 18 CORPORATION

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

I. Oil of Eucalyptus

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Oil of Eucalyptus PC Code: 040503
- Oil of Eucalyptus:
  - CAS#: 8000-48-4

Other Chemical Names: N/A

- Technical registrants: UNITED INDUSTRIES CORP.
- First approved for use in a registered product as a biochemical classified insecticide/repellent in 1948.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Oil of Eucalyptus is a volatile oil from the fresh leaves of Eucalyptus globulus and some other species of Eucalyptus. It is almost insoluble in water, but soluble in alcohol. It is miscible with absolute alcohol, oils and fats. It is composed mostly (70-80%) of eucalyptol, alpha pinene, phallandrene, terpineol, citronellal, geranyl acetate, eudesmol, eudesmyl acetate, piperitone, and volatile isovaleric aldhydes.

Use Information

- Use Sites: Oil of Eucalyptus is an active ingredient in products registered for use on pets.
- Target pest: Fleas and insects
- Application Methods: The products are applied in various ways. The products are sprayed or applied by hand, in a form of a lotion, or a trash bag.
- There are currently six biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED) was issued in December 1993 for Flower and Vegetable Oils which included Oil of Eucalyptus.

Human Health Risk Assessment

Oil of Eucalyptus was first registered in 1948 as a biochemical pesticide. There have been reported incidents for Oil of Eucalyptus See Incident section on page 30 of this document. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Oil of Eucalyptus have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Oil of Eucalyptus is

naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
305-56	REPEL ESSENTIAL INSECT REPELLENT LOTION	305	UNITED INDUSTRIES CORP.
305-57	REPEL ESSENTIAL INSECT REPELLENT PUMP SPRAY	305	UNITED INDUSTRIES CORP.
305-59	CITRIODIOL	305	UNITED INDUSTRIES CORP.
305-62	REPEL INSECT REPELLENT 30 LE	305	UNITED INDUSTRIES CORP.
73291-1	API LIFE VAR	73291	CHEMICALS LAIF
85589-1	MINT-X TRASH BAGS	85589	JAD CORPORATION OF AMERICA

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

J. Oil of Orange

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Oil of Orange PC Code: 0040517
- Oil of Orange:
  - CAS#: 8008-57-9

  Other Chemical Names: Oils, Orange, sweet
- Technical registrants: N/A (Registrant for EP with highest AI concentration: BAKER'S & 18 CORPORATION)

- First approved for use in a registered product as a biochemical classified insecticide/repellent in 1973.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Oil of Orange is a volatile oil expressed from fresh peel ripe fruit of the orange (Citrus aurantium var. sinensis L., Rutaceae that gives distinctive odors or flavor to plant, flower, or fruit. It was originally considered an essential oil. It consists of about 90% d-limonene, citral, decyl aldehyyde, methyl anthranilate, linalool, and terpineol. Oil of Orange is commonly used in food flavoring and cosmetics and is listed by FDA as GRAS per (21 CFR 182.20).

Use Information

- Use Sites: Oil of Orange is an active ingredient in products registered for use on ornamental plants, homes, and garbage dumps to repel dogs and cats.
- Target pest: Dogs and cats
- Application Methods: The products are applied in various ways. It is applied as an aroma pouch or as a pellet/tablet.
- There are currently two biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED) was issued in December 1993 for Flower and Vegetable Oils which included the review of Oil of Orange.

Human Health Risk Assessment

Oil of Orange was first registered in 1973 as a biochemical pesticide. Oil of Orange is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There are no incident reports on file with EPA for Oil of Citronella. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Oil of Orange have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active

ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Oil of Orange is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
74693-1	SCENT-OFF AROMA POUCHES	74693	BAKER'S & 18 CORPORATION
74693-2	SCENT-OFF PELLETS	74693	BAKER'S & 18 CORPORATION

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

K. Jojoba Oil

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Jojoba Oil PC Code: 067200
- Jojoba Oil:
  - CAS#: 61789-91-1

  Other Chemical Names: N/A
- Technical registrants: N/A (Registrant for EP with highest AI concentration: IJO PRODUCTS, LLC)
- First approved for use in a registered product as a biochemical classified insecticide/fungicide in 1996.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Jojoba oil is the liquid wax esters produced in the seed of the jojobas (Simmondsia Chinensis) plant. The oil makes up approximately 50% of the jojoba seed

by weight. It appears as a clear golden liquid at room temperature with a slightly fatty odor. Jojoba Oil is a fungicide registered for use for controlling mildew and an insecticide registered for use for controlling whiteflies.

Use Information

- Use Sites: Jojoba Oil is an active ingredient in products registered for use as a fungicide on ornamental plants, roses, strawberries, tomatoes, and registered as an insecticide on vegetable crops.
- Target pest: Whiteflies and powdery mildew
- Application Methods: The products are applied in by a tank sprayer on in a RTU spray solution
- There are currently two biochemical pesticide registrations.

Recent Actions

There have been no recent significant regulatory activities regarding Jojoba Oil (i.e., tolerance related actions, changes of use patterns, submission of toxicological studies or incident reports).

Human Health Risk Assessment

Jojoba Oil was first registered in 1996 as a biochemical pesticide. Jojoba oil is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There are no incident reports on file with EPA for Jojoba Oil. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Jojoba Oil have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Jojoba Oil is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low

toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
68186-2	E-RASE READY-TO-USE	68186	IJO PRODUCTS, LLC
68186-1	DETUR	68186	IJO PRODUCTS, LLC

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

L. Eugenol

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Eugenol PC Code: 102701
- Eugenol:
  - CAS#: 97-53-0

  Other Chemical Names: 4-Allyl-2-methoxyphenol
  Phenol, 2-methoxy-4-(2-propenyl)-

- Technical registrants: N/A (Registrant for EP with highest AI concentration: SUTERRA LLC)
- First approved for use in a registered product as a biochemical classified insecticide/attractant in 1983.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Eugenol is an allyl chain-substituted guaiacol. It is a member of the phenylpropanoids class of chemical compounds. It is clear to pale yellow oily liquid extracted from certain essential oils especially from clove oil, nutmeg, cinnamon, basil, and bay leaf. Eugenol is slightly soluble in water and soluble in organic solvents. It has a pleasant, spicy, clove-like aroma. Eugenol is used in perfumery and flavoring and also used in formulating insect attractants and UV absorbers, analgesics, biocides and antiseptics.

Use Information

- Use Sites: Eugenol is an active ingredient registered for use on many food crops; ornamentals; buildings; inside and outside and pets as an attractant and repellent.
- Target pest: Japanese Beetles, dogs and cats.
- Application Methods: The products are applied in various ways a bait trap or as a pressurized liquid.
- There are currently thirteen biochemical pesticide registrations.

Recent Actions

There have been no recent significant regulatory activities regarding Eugenol Oil (i.e., tolerance related actions, changes of use patterns, submission of toxicological studies or incident reports.)

Human Health Risk Assessment

Eugenol was first registered in 1983 as a biochemical attractant. Eugenol is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There have been reported incidents for Eugenol. See Incident section on page 30 of this document. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Eugenol have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Eugenol is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
84565-1	BULL RUN JAPANESE & ORIENTAL BEETLE TRAP	84565	BULL RUN SCIENTIFIC, VBT
73825-2	ECOZAP CRAWLING AND FLYING INSECTICIDE	73825	BIOGANIC SAFETY BRANDS, INC.
73825-1	ECOZAP WASP & HORNET INSECTICIDE	73825	BIOGANIC SAFETY BRANDS, INC.
67425-5	ECOPCO JET CONTACT INSECTICIDE	67425	ECOSMART TECHNOLOGIES, INC.
56336-8	SUREFIRE JAPANESE BEETLE TRAP	56336	SUTERRA LLC
51934-6	TRECE JAPANESE BEETLE TRAP	51934	TRECE, INC.
51934-2	JAPANESE BEETLE BAIT II	51934	TRECE, INC.
8845-129	JAPANESE BEETLE COMBO BAIT	8845	SPECTRUM GROUP
8845-48	BAG-A-BUG JAPANESE BEETLE TRAP	8845	SPECTRUM GROUP
8730-57	LURE N KILL JAPANESE BEETLE	8730	ABERDEEN ROAD COMPANY
4822-534	RAID EO ARK	4822	S.C. JOHNSON & SON INC.

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

M. Balsam Fir Oil

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Balsam Fir Oil PC Code: 129035
  Balsam Fir Oil:

- CAS#: 8021-28-1

Other Chemical Names: Fir Needle

- Technical registrants: N/A (Registrant for EP with highest AI concentration: EARTH KIND, INC.)
- First approved for use in a registered product as a rodent repellent biochemical classified in 2007.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Balsam Fir Oil is a pale yellow to amber liquid with a fresh woodsy scent. Balsam Fir Oil is a technical grade active ingredient (TGAI) in the manufacturing use product MP) Canadian Wilderness Oil and the end use product (EP) Fresh Cab®. This product is a non-food use biochemical pesticide that repels rodents in non-living spaces by emitting an odor.

Use Information

- Use Sites: Balsam Fir Oil as an active ingredient registered as a manufacturing use product (MP); and an end use product(EP), for use as a rodent repellent indoors in non-living areas (attics, basements, storage areas, garages, sheds, pantries, and barns) and in other enclosed spaces (such as automobiles, recreational vehicles, airplanes, boats, tractors, trucks and electric junction boxes). Target pest: Rodents
- Application Methods: The (EP) product, the pesticide is applied as one pouch per square feet of area (for indoor use) and four pouches per storage unit per season (for enclosed space).
- There are currently two biochemical pesticide registrations.

Recent Actions

A Biopesticides Registration Action Document (BRAD) has been prepared for Balsam Fir Oil.

Human Health Risk Assessment

Balsam Fir Oil was first registered in 2007 as a biochemical pesticide. Balsam Fir Oil is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There are no incident reports on file with EPA for Balsam Fir Oil.(February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Balsam Fir Oil have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Balsam Fir Oil is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
82016-2	CANADIAN WILDERNESS OIL	82016	EARTH KIND, INC.
82016-1	FRESH CAB	82016	EARTH KIND, INC.

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlabl/ppls.home.

N. Bergamot Oil

Background Information

Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Bergamot Oil PC Code: 129029
- Bergamot Oil:
  - CAS#: 8007-75-8

Other Chemical Names: N/A

- Technical registrants: N/A (Registrant for EP with highest AI concentration: BAKER'S & 18 CORPORATION)

- First approved for use in a registered product as a repellent biochemical classified in 1972.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Bergamot Oil is a volatile oil expressed from the rind of fresh fruit citrus aurantium L., var. bergamia It is used in cosmetics as perfumes and is popular in aromatherapy. It can be used in foods, as a fragrance and as a companion plant. Bergamot Oil is an active ingredient in products registered for use as a repellent for dogs and cats on ornamentals plants, homes, and garbage cans. It is also considered by FDA as GRAS (Generally Recognized As Safe) per 21 CFR 182.20.

Use Information

- Use Sites: Bergamot is registered for use on ornamental plants, homes and garbage cans.
- Target pest: Cats and dogs.
- Application Methods: The products are formulated as impregnated solid material or pellets.
- There are currently two biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED) was prepared in December 1993 for Flower and Vegetable Oils which included Bergamot Oil.

Human Health Risk Assessment

Bergamot Oil was first registered in 1972 as a biochemical pesticide. Bergamot Oil is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There are no incident reports on file with the Agency for Bergamot Oil. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Bergamot Oil have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active

ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Bergamot Oil is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
74693-1	SCENT-OFF AROMA POUCHES	74693	BAKER'S & 18 CORPORATION
74693-2	SCENT-OFF PELLETS	74693	BAKER'S & 18 CORPORATION

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

O. Geraniol

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Geraniol PC Code:597501
- Geraniol;
  - CAS#: 106-24-1

  Other Chemical Names: E)-Nerol
  2,6-Octadien-1-ol, 3,7-dimethyl-, (E)-
  Geranyl
  trans-3,7-Dimethyl-2,6-octadien-1-ol
  trans-Geraniol

Technical registrants: N/A (Registrant for EP with highest AI concentration: ARYSTA LIFESCIENCE NORTH AMERICA, LLC)

- First approved for use in a registered product as a biochemical classified repellent in 1972.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Geraniol is a monoterpenoid and an alcohol. It is the primary part of rose oil, palmarosa oil, and citronella oil (Java type). It also occurs in small quantities in geranium, lemon, and many other essential oils. It appears as a clear to pale-yellow oil that is insoluble in water, but soluble in most common organic solvents. It has a rose-like odor and is commonly used in perfumes. It is also used in flavors. Geraniol is an active ingredient in product registered for use as a Japanese beetle attractant and dog and cat repellent.

Use Information

- Use Sites: Geraniol is registered for use as an attractant on fruits, vegetables, ornamentals, homes and garbage dumps.
- Target pest: Japanese beetles, dogs and cats.
- Application Methods: The products are formulated as impregnated solid material or pellets .
- There are currently eleven biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED) was issued in December 1993 for Flower and Vegetable Oils which included Geraniol.

Human Health Risk Assessment

Geraniol was first registered in 1948 as a biochemical pesticide. Geraniol is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There have been reported incidents for Geraniol. See Incident section on page 30 of this document. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Geraniol have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Geraniol is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from

this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
84565-1	BULL RUN JAPANESE & ORIENTAL BEETLE TRAP	84565	BULL RUN SCIENTIFIC, VBT
74693-2	SCENT-OFF PELLETS	74693	BAKER'S & 18 CORPORATION
74693-1	SCENT-OFF AROMA POUCHES	74693	BAKER'S & 18 CORPORATION
70057-1	Biomite	70057	NATURAL PLANT PROTECTION S.A.
66330-390	SHOOTER INSECTICIDE	66330	ARYSTA LIFESCIENCE NORTH AMERICA, LLC
56336-8	SUREFIRE JAPANESE BEETLE TRAP	56336	SUTERRA LLC
51934-6	TRECE JAPANESE BEETLE TRAP	51934	TRECE, INC.
51934-2	JAPANESE BEETLE BAIT II	51934	TRECE, INC.
8845-129	JAPANESE BEETLE COMBO BAIT	8845	SPECTRUM GROUP
8845-48	BAG-A-BUG JAPANESE BEETLE TRAP	8845	SPECTRUM GROUP
8730-57	LURE N KILL JAPANESE BEETLE	8730	ABERDEEN ROAD COMPANY

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

P. Alpha-Ionone

Background Information

Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201
- Alpha-Ionone PC Code: 129030
- Alpha-Ionone:
  - CAS#: 127-41-3

  Other Chemical Names: N/A
- Technical registrants: N/A (Registrant for EP with highest AI concentration: BAKER'S & 18 CORPORATION)
- First approved for use in a registered product as a biochemical classified insecticide/repellent in 1965.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Alpha Ionone is from volatile oil of the plant Boronia megastigma Nees., Rutaceace; or can be produced synthetically. Alpha Ionone is an active ingredient in products registered for use as a repellent in dogs and cats repellent, and an attractant to adult rose chafers (a beetle). Alpha-Ionone products are used outdoors only. It is applied to plants and inanimate objects. It is also known as Irisone. Irisone is used in cosmetics as a perfume. Alpha-Ionone is also allowed in food for humans' consumption as a direct food additive.

Use Information

- Use Sites: Alpha-Ionone is registered for use outdoors only on plants and inanimate objects, e.g., lawn furniture.
- Target pest: Adult rose chafers (a beetle) and dogs and cat.
- Application Methods: The products are in the form of impregnated solid material or pellets.
- There are currently two biochemical pesticide registrations.

Recent Actions

A Reregistration Eligibility Document (RED) was issued in December 1993 for Flower and Vegetable Oils which included Alpha-Ionone.

Human Health Risk Assessment

Alpha-Ionone was first registered in 1965 as a biochemical pesticide. Alpha – Ionone is a naturally-occurring substance that has a non-toxic mode of action which has a

significant history of exposure to humans and the environment. There are no incident reports on file with EPA for Alpha-Ionone. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Alpha-Ionone have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Alpha-Ionone is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
74693-1	SCENT-OFF AROMA POUCHES	74693	BAKER'S & 18 CORPORATION
74693-2	SCENT-OFF PELLETS	74693	BAKER'S & 18 CORPORATION

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

Q. Oil of Thyme

Background Information
Vegetable and Flower Oils registration review case number: 8201

- Vegetable and Flower Oils registration review case number: 8201

- Oil of Thyme PC Code: 597800
- Oil of Thyme:
  - CAS#: 8007-46-3

  Other Chemical Names: N/A
- Technical registrants: N/A (Registrant for EP with highest AI concentration: ARYSTA LIFESCIENCE NORTH AMERICA, LLC)
- First approved for use in a registered product as a biochemical classified insecticide/repellent in 2004.
- Biopesticide and Pollution Prevention Registration Review Lead: Menyon Adams, adams.menyon@epa.gov

Description of Active Ingredient

Oil of Thyme is a pesticide active ingredient in products registered for use in controlling aphids on ornamental plants in ponds and other aquatic sites. It is also a common herb used for flavoring food. It has no known harmful effects to living organisms or the environment.

Use Information

- Use Sites: Oil of Thyme is registered for use on ponds, fountains, aquaria, and other aquatics as a repellent.
- Target pest: Aphids
- Application Methods: The product is sprayed on the exposed parts of the plants, left to sit five minutes, and then washed away with the dead aphids using a water spray.
- There are currently one biochemical pesticide registrations.

Recent Actions

There have been no recent significant regulatory activities regarding Oil of Thyme (i.e., tolerance related actions, changes of use patterns, submission of toxicological studies or incident reports.)

Human Health Risk Assessment

Oil of Thyme was first registered in 2004 as a biochemical pesticide. Oil of Thyme is a naturally-occurring substance that has a non-toxic mode of action which has a significant history of exposure to humans and the environment. There are no incident reports on file with the Agency for Oil of Thyme. (February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist)

Environmental Fate and Ecological Risk Assessment Status

The Agency does not anticipate the need for additional environmental fate data for this registration review. The environmental fate data for Oil of Thyme have been satisfied due to the low concentration of the active ingredient in the end use products, low use volume and rapid degradation in the environment by normal biological, physical, and/or chemical processes that can be reasonably expected to exist where the pesticides are applied. In each case, non-target data and/or various non-target scientific rationales were sufficient to determine that the proposed uses of the pesticides containing this active ingredient posed negligible to non-existent ecological risk. EPA's ecological risk assessments to date are supported by the understanding that Oil of Thyme is naturally-occurring and regarded as practically non-toxic to non-target mammals, birds, and plants. Due to the non-toxic mode of action and lack of exposure to non-target organisms from this product, a Risk Quotient (RQ) is not typically calculated since the point estimates of either toxicity or exposure will be at or near zero. No contact toxicity has been reported. No ecological incidents were reported. Therefore, the Agency does not foresee the need for additional ecotoxicity data for a new risk assessment for this registration review. Ecological effects data requirements were fulfilled by scientific rationales due to the low toxicity and low exposure from the use patterns. (February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist)

Labels and Products

Registration #	Registration Name	Company #	Company Name
66330-390	SHOOTER INSECTICIDE	66330	ARYSTA LIFESCIENCE NORTH AMERICA, LLC

Labels for the above products can be obtained from the Pesticide Product Label System (PPLS) website: http://oaspub.epa.gov/pestlab1/ppls.home.

III. GLOSSARY of TERMS & ABBREVIATIONS

ai	Active Ingredient
AR	Anticipated Residue
ASTM	American Society for Testing and Materials
AWPA	American Wood Preserver's Association
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formula
CSFII	USDA Continuing Surveys for Food Intake by Individuals
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
DNT	Developmental Neurotoxicity
DWLOC	Drinking Water Level of Comparison

EC	Emulsifiable Concentrate Formulation
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EUP	End-Use Product
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
GENEEC	Tier I Surface Water Computer Model
IR	Index Reservoir
LC_{50}	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD_{50}	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOC	Level of Concern
LOAEL	Lowest Observed Adverse Effect Level
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number). EPA's system of recording and tracking submitted studies.
MUP	Manufacturing-Use Product
NA	Not Applicable
NAWQA	USGS National Ambient Water Quality Assessment
NPDES	National Pollutant Discharge Elimination System
NR	Not Required
NOAEL	No Observed Adverse Effect Level
OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PAIRA	Pure Active Ingredient Radiolabelled
PCA	Percent Crop Area
PDP	USDA Pesticide Data Program
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
Q_1^*	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RAC	Raw Agriculture Commodity
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Tier I Ground Water Computer Model
SAP	Science Advisory Panel

SF	Safety Factor
SLN	Special Local Need (Registrations Under Section 24(c)) of FIFRA)
TGAI	Technical Grade Active Ingredient
TEP	Typical End-Use Product
USDA	United States Department of Agriculture
UF	Uncertainty Factor
WPS	Worker Protection Standard

IV. References

U.S. EPA (1993) Reregistration Eligibility Decision (RED) Flower and Vegetable Oils. Washington, DC, US Environmental Protection Agency

U.S. EPA Reregistration Eligibility Decision (RED) for Oil of Citronella

U.S. EPA Reregistration Eligibility Decision (RED) Fact Sheet for Oil of Citronella

U.S. EPA (1993) Reregistration Eligibility Decision (RED) Fact Sheet for Flower and Vegetable Oils

U.S. EPA (1993) Reregistration Eligibility Decision (RED) Fact Sheet for Plant Oils

U.S. EPA (2009) Biopesticides Registration Action Document (BRAD) Indole

U.S. EPA (2009) Indole Fact Sheet

U.S. EPA (2001) Plant Oils Fact Sheet

Wikipedia

FDA (2009) Code of Federal Regulations title 21

U.S. EPA (200) Biopesticides Registration Action Document (BRAD) Balsam Fir Oil

February 19, 2010, Preliminary Human Health Assessment for the Registration Review of Vegetable and Flower Oils, Sadaf Shaukat, Biologist

February 26, 2010, Non-Target Organism Studies, Hazard Assessment, and Endangered Species Assessment for the Vegetable and Flower Oils in Support of Registration Review, Jacob Moore, Chemist

GLP Test Facility
Metabolism & Environmental Fate Dept.
Via Fauser 28, 28100 Novara (Italy)

REPORT

CHARACTERIZATION OF ALLYL ISOTHIOCYANATE (AITC) OF SYNTHETIC AND NATURAL ORIGIN

February, 2013

Title

Characterization of Allyl Isothiocyanate (AITC) of synthetic and natural origin

Data requirements

Regulation (EC) No 1107/2009 and
Regulation (EC) No 544/2011 Part A, Section 1
EC Working Document SANCO/3030/99 rev.4 (11/07/00).

Author

Francesca Rizzo

Date

February 28, 2013

Testing Facility

ISAGRO – GLP Test Facility
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USA

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STATEMENT OF DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this document on the basis of its falling within the scope of FIFRA Section 10 (d)(1)(A), (B), or (C).

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Date

_____ _____

Date

This study is proprietary and is to be considered confidential and trade secret information in all countries except the United States of America, and for all purposes other than those enunciated in FIFRA Section 3 and Section 10.

SPONSOR

SPONSOR	ISAGRO USA Inc. Morrisville, NC 27560 USA

AUTHOR

Test Facility Director		date
Dr Francesca Rizzo Francesca Rizzo	ISAGRO Spa GLP Test Facility Metabolism & Environmental Fate Dept. Head	28 Feb 2013

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1. SUMMARY

An analytical method for determining the content of active ingredient in Allyl Isothiocyanate (AITC) technical product was developed and validated for specificity, linearity and precision, according to SANCO/3029/99 rev. 4 (11/07/2000).
The content of active ingredient in AITC technical product was assessed by GC/FID with split/splitless injection method.
Since AITC is present in equilibrium mixture with its isomer Allyl Thiocyanate (ATC), that quickly converts to the isomer by allylic rearrangement at the temperatures commonly used with the split/splitless injection system, the active ingredient content was determined as sum of AITC and ATC isomers. Then the actual ratio of the isomers was determined by ^{1}H-NMR.
Two AITC samples, batch#QJH1203012 of synthetic origin and batch#1050120806/11 of natural origin, were analysed for active ingredient content and characterized by GC/MS, ^{1}H-NMR, IR and UV/VIS spectroscopy. Refractive index, boiling point and density were also determined on both samples.

The gaschromatographic purity of the samples of synthetic and natural origin is 100% and 98.93% (w/w) respectively and the AITC/ATC isomer ratio is 96/4 for both samples.
GC/MS, ^{1}H-NMR, IR and UV/VIS spectra of the samples (synthetic and natural origin) are comparable.
Also refractive index, boiling point and density determined in both samples are comparable.
The comparison results are summarized in table below:

	batch#QJH1203012 **synthetic origin**	*batch#1050120806/11* **natural origin**
GC purity	100% (w/w)	98.93% (w/w)
NMR (AITC/ATC ratio)	96/4	96/4
GC/MS	comparable spectra	
^{1}H-NMR	comparable spectra	
IR	comparable spectra	
UV/VIS	comparable spectra	
refractive index (589 nm and 20°C)	1.531	1.532
boiling point	420 K (147°C)	422 K (149°C)
density	1.017 g/ml	1.016 g/ml

In conclusion AITC samples of synthetic and natural origin were confirmed to be authentical and have comparable chemical-physical characteristics.

2. OBJECTIVE

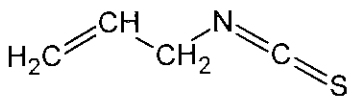
The present characterization was conducted to compare the AITC samples of synthetic and natural origin.

3. TEST ITEMS

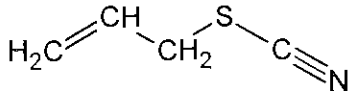
3.1. IDENTIFICATION

AITC technical product of synthetic origin	Batch#QJH1203012
AITC technical product of natural origin	Batch#1050120806/11

General characteristics of AITC and its isomer ATC:



AITC



ATC

IUPAC name:	3-isothiocyanato-1-propene	allyl thiocyanate
Molecular formula:	C_4H_5NS	
Molecular weight:	99.15	
CAS No:	57-06-7	764-49-8
Physical state:	colorless oil	

3.2. SOURCE

Batch#QJH1203012 was supplied by Quingdao Ji Ahua Chemical Company Ltd and Batch#1050120806/11 by Naturex (see Appendix A).

3.3. STORAGE

Test Items were stored at room temperature.

4. CHARACTERIZATION

Both batches of AITC (QJH1203012 of synthetic origin and 1050120806/11 of natural origin) were analysed for active ingredient content by GC/FID and ^{1}H-NMR and characterized by GC/MS, ^{1}H-NMR, IR (Infrared spectroscopy), refractive index, UV/VIS spectroscopy. Refractive index, boiling point and density were also determined on both samples.
Relevant study reports are attached in Appendices 1 to 7.

4.1. SOURCE OF DATA

- The analytical method for AITC was developed and validated by Renolab srl - Test Facility, Via Spinelli 12, 44028 Poggio Renatico (FE) – Italy
- ^{1}H-NMR analysis was performed by Chemistry Dept of Isagro SpA Centro Ricerche, Via Fauser 4, 28100 Novara – Italy
- GC/MS analysis was carried out by Process Development.Dept of Isagro SpA Centro Ricerche, Via Fauser 4, 28100 Novara – Italy
- IR analysis and determination of refractive index were performed by Redox snc Test Facility – Viale Stucchi 62/26 – 20052 Monza-Italy
- UV7VIS analysis and determination of density and boiling point were carried out by Renolab srl - Test Facility, Via Spinelli 12, 44028 Poggio Renatico (FE) – Italy

5. REFERENCES

- EC Working document SANCO/3030/99 rev. 4 (11/07/00)
- OECD guidelines 101, 103
- OPPTS guidelines series 830
- CIPAC 3.2

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6. APPENDICES

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6.1 Appendix A: Product specification of AITC of natural origin

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NATUREX
Ultimate Botanical Benefits

Product Specification

Ref : AA010801

MUSTARD ESSENTIAL OIL

This specification sheet cancels and replaces all previous publications : ***February 14, 2012***

- **Description :**

  Essential oil obtained by steam distillation from mustard seeds.

  Botanical name : *Brassica juncea L.*

- **Composition :**

  Natural extract

- **Regulations status :**

  Natural flavouring of the named source according to European Regulation 1334/2008/EC. Natural flavoring according to US Code of Federal Regulation 21CFR101.22.

- **Specifications :**

Sensory quality :

Aspect :	Liquid
Color :	Clear yellow
Flavor :	Characteristic of mustard, extremely penetrating, pungent
Solubility :	Oil and alcohol soluble

Analytical quality :

Specific gravity (20°C/20°C) :	1.01 - 1.03
Refractive index (20°C) :	1.52 - 1.54
Optical rotation (20°C) :	Inactive
Water content :	< 0.5 %
Allyl-(isothiocyanate + thiocyanate) content :	> 95%
Total isothiocyanates + thiocyanates content :	> 97%

Microbiological quality :

Total plate count :	< 1000 ufc/g
Yeasts and molds :	< 100 cfu/g

- **Packaging :**

  Aluminium bottle: 1 and 6 kg net

- **Storage conditions :**

  Temperature <12 °C, sheltered from light, moisture and oxygen.

- **Shelf life :**

  12 months under the previously mentioned conditions and in its original packaging.

GLOBAL HEADQUARTERS - Site d'Agroparc - BP 1218 - 84911 Avignon cedex 9 - France - Tel : 33 (0)4 90 23 96 89 - Fax : 33 (0)4 90 23 73 40
US HEADQUARTERS - 375 Huyler street - South Hackensack - NJ 07606 - USA - Tel: 1 201 440 5000 - Fax : 1 201 342 8000
E-mail : naturex@naturex.com - Website : www.naturex.com

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6.2 APPENDIX B: Development and validation of an analytical method for the determination of AITC in technical product

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Final Report

Development and Validation of an Analytical Method for the Determination of Allyl Isothiocyanate (AITC) in AITC Technical

Guideline(s)

SANCO 3030/99 rev. 4,
11/07/2000

Study Director

Sara Morsiani

Date

21 December 2012

Test Facility

Renolab S.r.l.
Via Spinelli, 12
I-44028 Poggio Renatico (FE)
Italy

Sponsor

ISAGRO S.p.A.
Centro Uffici San Siro Fabbricato D-ala 3
Via Caldera, 21
I-20153 Milano (MI)
Italy

Test item:
AITC Technical

Study code:
12070-01C

Statement of Confidentiality

This report contains confidential and proprietary information of ISAGRO S.p.A. which must not be disclosed to anyone except the employees of this company or to persons authorised by law or judicial judgement without the expressed and written approval of ISAGRO S.p.A.

Statement of Compliance with the Principles of Good Laboratory Practice

The study described in this report was conducted in compliance with the most recent edition of:

- Law Decree 2nd March 2007 N° 50 – Actuation of Directives 2004/9/EC and 2004/10/EC concerning the inspection and verification of Good Laboratory Practice (GLP) and aligning of laws, regulations and administrative provisions related to the application of the Principles of Good Laboratory Practice and to the control of their application for chemicals tests.
- The OECD Principles of Good Laboratory Practice.

The Italian requirements are based on the OECD Principles of Good Laboratory Practice which are accepted by regulatory authorities throughout the European Community, the United States of America (FDA and EPA) and Japan (MHW, MAFF and METI) on the basis of intergovernmental agreements.

This report fully and accurately reflects the procedure used and data generated.

Sara Morsiani
Study Director

21 DEC 2012
Date

Statement of Quality Assurance Unit

Study code:	12070-01C
Study title:	Development and Validation of an Analytical Method for the Determination of Allyl Isothiocyanate (AITC) in AITC Technical

Study plan was verified and experimental phase, draft report and final report of this study were audited by the Quality Assurance in compliance with the OECD Guidelines and to Renolab's Standard Operating Procedures.

The dates are given below:

Phase or document inspected	Date of audit/ verification	Date of report to			
		Principal Investigator	Test site Management	Study Director	Test Facility Management
Study plan:	21 Nov 2012	n.a.	n.a.	n.a.	n.a.
Experimental analytical phase:	23 Nov 2012	n.a.	n.a.	26 Nov 2012	26 Nov 2012
Draft Final report:	20 Dec 2012	n.a.	n.a.	21 Dec 2012	21 Dec 2012

The final report correspond to the raw data

Dr. Kimema Nyatemu
Quality Assurance

21 Dec 2012
Date

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List of Tables

List of Figures

1 Summary

An analytical method (MA CCF 141-1) for determining the content of active ingredient in the Allyl Isothiocyanate (AITC) Technical was validated with respect to specificity, linearity of detector response, and precision according to guideline SANCO 3030/99 rev. 4 (11/07/2000).

Method principle: The content of active ingredient in the Allyl Isothiocyanate (AITC) Technical was assessed by GC/FID whit split/splitless injection method.

Since AITC is present in equilibrium mixture with its isomer Allyl Thiocynate (ATC), that quickly converts to the isomer by allylic rearrangement at the temperatures commonly used with the split/splitless injection system, the active ingredient content was determined as sum of AITC and ATC isomers. Then the actual ratio of the isomers was determined with ^{1}H-NMR ("cold method").

Specificity: Allyl Isothiocyanate (AITC) and Allyl Thiocynate (ATC) were identified by retention time in comparison to a corresponding reference substance. Since GC/FID is not a highly specific method, a non-GLP confirmation of the Allyl Isothiocyanate (AITC) and Allyl Thiocyanate (ATC) identity in the test item was performed by ^{1}H-NMR.

Linearity: The linearity of the detector response was demonstrated by analyzing test item solutions (duplicate independent determinations) at the nominal content, -20 % nominal content and + 20 % nominal content of test item and plotting the detector response versus the test item weighed amount (mg). The correlation coefficient (r) was found to be 0.9980.

Precision: The method precision was assessed as relative standard deviation (RSD %) for the whole procedure of sample preparation and measurement of five extracts.

The precision determined was 1.22 % and fell within the limits given in SANCO/3030/99 rev.4 by the modified Horowitz equation.

Purity: The a.i. content in the test item (purity), determined concurrently with precision, resulted 100.5 ± 1.2 % as sum of AITC and ATC isomers. Moreover the ^{1}H-NMR analysis revealed a 96:4 ratio between AITC and ATC in the test item at ambient temperature.

2 Time Schedule

Study plan authorisation:	21 November 2012
Start of experimental phase:	23 November 2012
End of experimental phase	27 November 2012
Draft report:	19 December 2012
Study completion date	21 December 2012

3 Study Objective

The aim of this study was to validate the analytical method for determining the active ingredient content (purity) in Allyl Isothiocyanate (AITC) Technical to meet the requirements of guidelines SANCO/3029/99 rev. 4 (11/07/2000).

4 Materials and Methods

4.1 Test Item

Name:	Allyl Isothiocyanate (AITC) Technical
Active ingredient(s) (common name and synonym)	Allyl Isothiocyanate (AITC) or oil of mustard
Active ingredient(s) IUPAC name:	3-isothiocyanatoprop-1-ene
CAS Number of a.i.(s):	57-06-7
Purity (nominal):	> 96 %
Physical state:	Limpid orange liquid
Supplier:	ISAGRO RICERCA S.r.l.
Batch number:	QJH120312
Renolab Code:	12070
Expiry date:	September 2014
Storage conditions:	Room temperature

4.2 Reference Item(s)

Name:	Allyl Isothiocyanate (AITC)
Synonym:	Allyl Isothiocyanate (AITC) or oil of mustard
IUPAC name	3-isothiocyanatoprop-1-ene
CAS No.:	57-06-7
Supplier:	Sigma Aldrich
Renolab code:	SR 220
Batch number:	SZBC285XV
Purity:	95.5 %[(1)]
Expiry:	11 October 2015
Storage:	Refrigerator, nominally 4-10 °C

[(1)]This value was reported on the Sigma Aldrich certificate of analysis (Appendices, Figure 10): since Allyl Isothiocyanate (AITC) is present in equilibrium mixture with its isomer Allyl Thiocynate (ATC), that quickly converts to the isomer by allylic rearrangement at the temperatures commonly used with the split/splitless injection system (References, point 2), a purity check was performed on SM 220-2 (see Section 4.6) to verify the reference item purity in the instrumental conditions under validation. The resulting reference item purity was then 100 % as sum of AITC and ATC (Appendices, Figure 2).

4.3 Equipment

- Standard laboratory glassware
- Analytical Balance accurate to 0.1 mg, mod. AT 261, Mettler-Toledo
- Gas chromatograph equipped with split/splitless injector, autosampler, column oven and FID detector, mod. Autosystem XL, Perkin Elmer
- GC capillary column 0.32 mm internal diameter, 0.25 µm film thickness, 30 m length, Supelcowax 10, Supelco

- ^{1}H-NMR spectrometer 300MHz, Brucker (equipment of Isagro Ricerca Chemistry Department)

4.4 Reagents and Materials

- n-hexadecane, Sigma Aldrich
- Dichloromethane, Sigma Aldrich
- Deuterated chloroform (used for ^{1}H-NMR spectrum by Isagro Ricerca Chemistry Department)

4.5 Reagent Solutions Preparation

Internal standard solution, n-hexadecane 1.5 mg/mL in dichloromethane: 303.1 mg of n-hexadecane were accurately weighed and transferred in a 200 mL volumetric flask; then diluted to volume with dichloromethane to give a 1.5 mg/mL n-hexadecane internal standard solution.

4.6 Reference Item Solutions

Reference item stock solution SM 220-2 was prepared by weighing 22.5 mg of Allyl Isothiocyanate, batch SZBC285XV in a 2 mL volumetric flask and making up to volume with dichloromethane. This stock solution was used for the reference item purity check.

Reference item stock solution SM 220-3 was prepared by weighing 75.3 mg of Allyl Isothiocyanate, batch SZBC285XV in a 5 mL volumetric flask and making up to volume with n-hexadecane 1.5 mg/mL in dichloromethane internal standard solution to give a 15.060 mg/mL (sum of isomers) refererence item solution.

Reference item stock solution SM 220-4 was prepared by weighing 74.7 mg of Allyl Isothiocyanate, batch SZBC285XV in a 5 mL volumetric flask and making up to volume with n-hexadecane 1.5 mg/mL in dichloromethane internal standard solution to give a 14.940 mg/mL (sum of isomers) refererence item solution.

Reference item stock solution SM 220-5 was prepared by weighing 78.5 mg of Allyl Isothiocyanate, batch SZBC285XV in a 5 mL volumetric flask and making up to volume with n-hexadecane 1.5 mg/mL in dichloromethane internal standard solution to give a 15.700 mg/mL (sum of isomers) refererence item solution.

Reference item stock solutions injections were interspersed with test item solutions injections ad used to calculate the active ingredient content in Allyl Isothiocyanate Technical by a bracketing procedure.

In Appendices, Figure 5 and 6 were reported examples of chromatograms of test item solutions for linearity.

4.7 GC-FID analysis

GC-FID system:	Perkin Elmer, Autosystem XL
Analytical Column:	Supelcowax 10, 30.0 m x 0.32 mm id, film 0.25 µm
Oven:	80 °C, hold 2 minutes to 160 °C 5 °C/min, hold 0.10 min to 240 °C 20 °C/min, hold 2 min
Run time:	24.10 minutes
Carrier gas:	Helium 1.0 mL/min (constant flow)
Inlet:	Split mode
	280 °C
	split flow 50 mL/min
Injection volume:	1 µL
FID Detector:	280 °C
Retention times:	AITC: 6.3 min
	ATC: 8.0 min
	n-hexadecane: 10.9 min

4.8 Analytical procedure

Around 150 mg of test item were accurately weighed into a 10 mL volumetric flask and then made up to volume with n-hexadecane 1.5 mg/mL in dichloromethane internal standard solution. Then the test item solution was transferred in a vial and GC/FID analysed.

4.9 Calculations

The concentration of AITC/ATC sum of isomers $CONC_{FOUND}$ in the test item solutions was calculated as follows by comparison of the test item solution response with the response of the reference item stock solution injected before and after (bracketing procedure):

$$CONC_{FOUND}(mg/mL) = \frac{CONC_{STD} \times AR_{sample}}{AR_{STD}}$$

Where:

$CONC_{STD}$ = concentration (mg/mL) of the bracketing reference item stock solution

AR_{sample} = internal standard response ratio of the AITC/ATC sum area of isomers in the analytical sample

AR_{STD} = internal standard response ratio of the AITC/ATC sum area of isomers in the reference item stock solution injected before and after the sample (mean value).

Then the purity the test item was calculated as follows:

$$Purity\ (\%) = \frac{CONC_{FOUND} \times V}{W} \times 100$$

Where:

$CONC_{FOUND}$ = concentration of AITC/ATC sum of isomers in the test item solution

V = volume of the test item solution

W = sample weight

All the data reported in the tables of this report are rounded values taken from Excel spreadsheets which will be archived with the raw data. The use of Excel spreadsheets to make the calculations produces more accurate endpoints. These endpoints may occasionally slightly differ from the values derived by substituting the rounded values in calculations.

5 Amendment/Deviations to the study plan

The study was performed according to Study Plan 12070-01C dated 21 November 2012. This report reflects the conduct of this study.

6 Results

6.1 Specificity

The retention times of Allyl Isothiocyanate (AITC) and Allyl Thiocyanate (ATC) isomers in the test item solutions matched the retention times of the components of the analytical standard (Appendices, Figure 4 and Figure 7).

Since GC/FID is not a highly specific method , a non-GLP confirmation of the Allyl Isothiocyanate (AITC) and Allyl Thiocyanate (ATC) identity in the test item was performed with NMR by Dr Marilena Gusmeroli, Chemistry Department - Isagro Ricerca. This test was performed by diluting a suitable amount of test item in deuterated chloroform and analysing by ^{1}H-NMR spectroscopy. The presence of the AITC and ATC isomers was pointed out by the chemical shift (δ) and splitting of ^{1}H-NMR signals related to $-CH_2$ group and H_a, $H_{a'}$, H_b, $H_{b'}$ hydrogens (Appendices, Figure 8). In the following table (Table 1) was described and discussed the ^{1}H-NMR spectrum of the test item, Allyl Isothiocyanate (AITC) Technical, batch QJH120312 which is reported in Appendices, Figure 9.

Table 1: Discussion of ^{1}H-NMR spectrum of the test item

Test item	Batch	Chemical Shift (δ) (ppm)	Integration	Assignment
Allyl Isothiocyanate Technical	QJH120312	1.5	trace	water
		3.5-3.6	5.932	CH_2-ATC
		4.1-4.2	143.265	CH_2-AITC
		5.2-5.5	143.152	H_a $H_{a'}$
		5.8-6.0	70.604	H_b $H_{b'}$

Since ^{1}H-NMR is a "cold" method, the ratio between the CH_2-AITC and CH_2-ATC signals also yielded the actual ratio (i.e. at ambient temperature) between the AITC and ATC isomers that resulted 96-4 respectively.

6.2 Linearity

The linearity of the detector response was demonstrated by analyzing test item solutions (duplicate independent determinations) at the nominal content, -20 % nominal content and + 20 % nominal content of test item and plotting the detector response versus the test item weighed amount (mg). The analytical system of AITC/ATC sum of isomers gave a linear response for test item weighing amounts between 120 and 180 mg in dichloromethane with 1.5 mg/mL n-hexadecane internal standard. The linear correlation coefficient of the regression line (r^2) was found to be > 0.99 fulfilling the requirements of SANCO/3030/ rev. 4. The linearity plot is reported in Appendices, Figure 1.

The linearity range comprised the concentration range of the samples ± 20 %.

6.3 Precision and a.i. content

The repeatability test was performed by processing five independent samples prepared as described in section 4.8: each extract was injected twice. Results, reported in Table 2, were used to determine the following precision.

Purity as sum of AITC and ATC isomers (mean): 100.5 ± 1.2 % w/w RSD % = 1.22

The ambient temperature ratio between the AITC and ATC isomer in the test item was determined by ^{1}H-NMR "cold method" by mean of the ratio between CH_2-AITC and CH_2-ATC signals and resulted 96-4 respectively.

Results of precision determination, fell within the limits given in SANCO/3030/99 rev.4.

Table 2: Data and results method precision

Det n°	Sample weight mg	Sample volume mL	Dilution	AITC purity as sum of isomers % w/w
1	153.3	10	1	101.3 100.8
2	149.4	10	1	101.5 99.8
3	154.9	10	1	100.5 101.8
4	155.5	10	1	99.1 102.2
5	153.7	10	1	98.5 99.8

A representative chromatogram of a test item solution was reported in Appendices, Figure 7.

7 Discussion and Conclusions

The analytical method, which was assigned the Renolab code MA CCF 141-1, was validated for specificity, linearity and repeatability.

Allyl Isothiocyanate (AITC) and the isomer Allyl Thiocynate (ATC) were identified by retention times in comparison to a corresponding reference substance. Moreover a non-GLP confirmation of the two isomers identity in the test item was performed with ^{1}H-NMR.

The linear correlation coefficient (r^2) for the ± 20 % test item nominal content in the samples was found to be > 0.99 fulfilling the requirements of SANCO/3030/ rev. 4.

The relative standard deviations of the precision determination for the test item purity determination was 1.22 %, within the proposed acceptability assessed by Horowitz equation.

The a.i. content, determined concurrently with precision, resulted 100.5 ± 1.2 % as sum of AITC and ATC isomers. Moreover the ^{1}H-NMR analysis revealed a 96:4 ratio between AITC and ATC in the test item at ambient temperature.

The data presented in this report demonstrate that the analytical method provides a specific, reliable and precise procedure for the purity determination of Allyl Isothiocyanate (AITC) Technical.

8 Archiving

For the periods demanded by the principles of GLP the following documents and materials will be archived:

- Study plan, raw data and the final report (10 years).
- All documentation generated by the Quality Assurance Unit (10 years).
- A sample of test item and reference items (1 year).

All documents and materials will be stored in the archives of Renolab S.r.l. The premises for storing the documents and materials are settled according to the principles of Good Laboratory Practice in the organisation of the testing facility.

9 Reference (s)

1 Technical Material and Preparations, Guidance for generating and reporting methods of analysis in support of pre - and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414, European commission, SANCO/3030/99 rev.4, 11/07/00.

2 Antimicrobial Properties of Sinigrin and its hydrolysis properties, B. G. Shofran, S. T. Purrington, F. Breidt and H. P. Fleming, Journal of Food Science, Volume 63, No 4, 1998

10 Distribution

	Study Plan	Raw Data	Final Report
Sponsor	1 original	-	1 original
Test Facility:	1 original	1 original	1 original

11 Appendices

11.1 Linearity Curve(s)

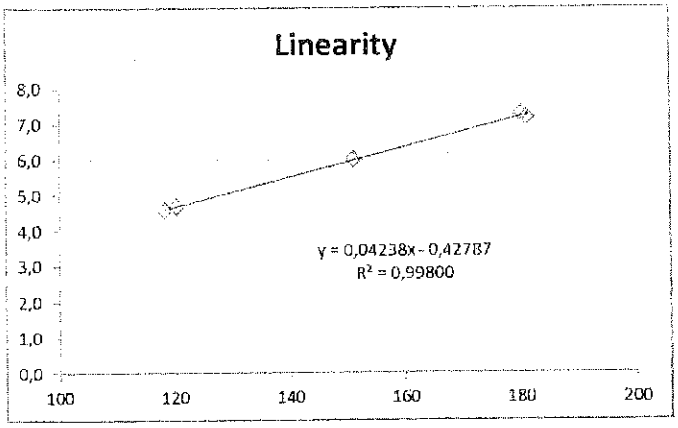

Figure 1: Linearity curve of AITC and ATC sum of isomers in AITC Technical.

11.2 Representative Chromatograms

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Sample Name	: SM 220-2 Pur Check	Data Acquisition Time	: 11/23/2012 5:33:59 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/2	Operator	: lg
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 2		

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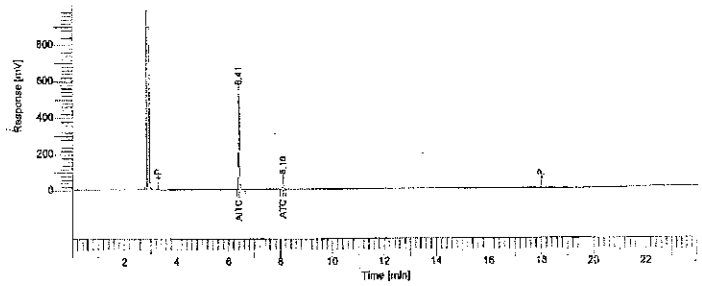

Allyl Isothiocyanate Purity

Peak #	Component Name	Time [min]	Area [uV*sec]	Area [%]
1	AITC	6.41	1431315	92.07
2	ATC	8.10	123359	7.93
			1554675	100.00

Figure 2: Purity check of Allyl Isothiocyanate reference item, batch SZBC285XV, Sigma-Aldrich

Software Version	: 6.2.1.0.104:0104	Date	: 11/27/2012 8:49:29 AM
Sample Name	: solvent DCM	Data Acquisition Time	: 11/23/2012 11:48:16 AM
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Sample Amount	: 1.000000	Dilution Factor	: 1.000000
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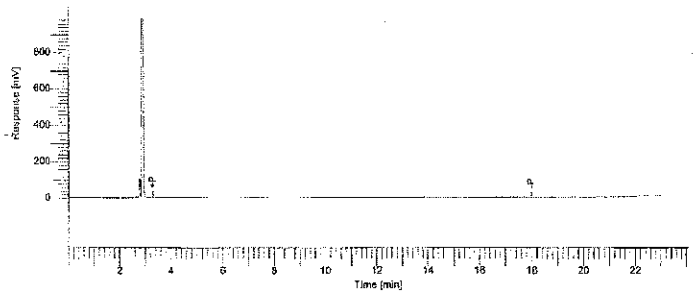

Allyl Isothiocyanate Technical

No peaks available to report
Missing Component Report

Component	Expected Retention (Calibration File)
AITC	6.390
ATC	8.090
n-hexadecane	11.110

Figure 3: Chromatogram of a dichloromethane (DCM) solvent injection

Software Version	: 6.2.1.0.104:0104	Date	: 11/27/2012 9:36:10 AM
Sample Name	: SM 220-3 (2)	Data Acquisition Time	: 11/23/2012 11:22:17 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/3	Operator	: lg
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 13		

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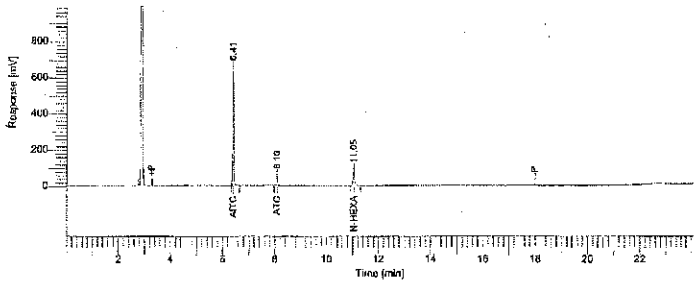

Allyl Isothiocyanate Technical

Peak #	Component Name	Time [min]	Area [uV*sec]	ISTD Resp Ratio
1	AITC	6.41	1763606	0.0000
2	ATC	8.10	151159	0.0000
3	n-hexadecane	11.05	327920	0.0000
			2242685	0.0000

Figure 4: Chromatogram of a 15.060 mg/mL as AITC/ATC sum of isomers reference item solution

Software Version	: 6.2.1.0.104:0104	Date	: 11/27/2012 8:49:34 AM
Sample Name	: Lin -20% TN-2	Data Acquisition Time	: 11/23/2012 2:27:15 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/6	Operator	: lg
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 6		

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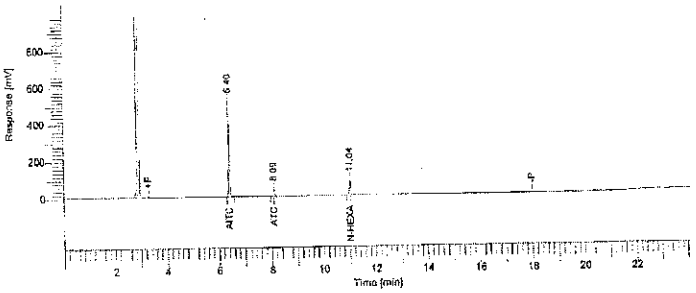

Allyl Isothiocyanate Technical

Peak #	Component Name	Time [min]	Area [uV*sec]	ISTD Resp Ratio
1	AITC	6.40	1397517	0.0000
2	ATC	8.09	120402	0.0000
3	n-hexadecane	11.04	324283	0.0000
			1842202	0.0000

Figure 5: Chromatogram of a 120.5 mg in 10 mL test item solution for linearity

Software Version	: 6.2.1.0.104:0104	Date	: 11/27/2012 8:49:33 AM
Sample Name	: Lin +20% TN-1	Data Acquisition Time	: 11/23/2012 1:55:28 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/5	Operator	: lg
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 5		

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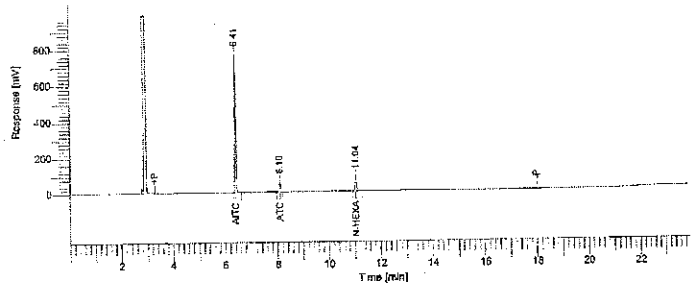

Allyl Isothiocyanate Technical

Peak #	Component Name	Time [min]	Area [uV*sec]	ISTD Resp Ratio
1	AITC	6.41	2086159	0.0000
2	ATC	8.10	180075	0.0000
3	n-hexadecane	11.04	316059	0.0000
			2582293	0.0000

Figure 6: Chromatogram of a 181.3 mg in 10 mL test item solution for linearity

Software Version	: 6.2.1.0.104:0104	Date	: 11/27/2012 9:38:09 AM
Sample Name	: Sample 5 (1)	Data Acquisition Time	: 11/23/2012 10:50:37 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/15	Operator	: lg
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 12		

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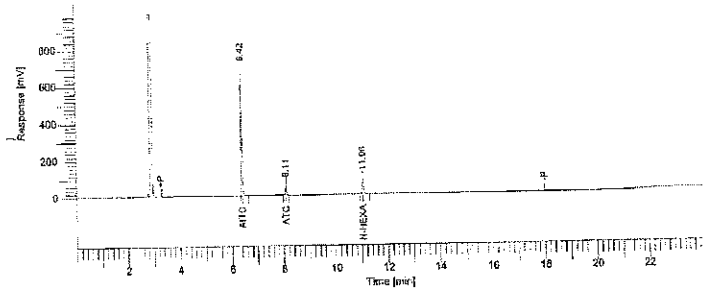
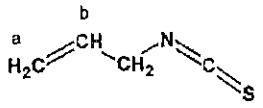


Allyl Isothiocyanate Technical

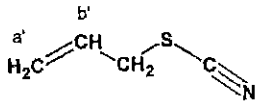
Peak #	Component Name	Time [min]	Area [uV*sec]	ISTD Resp Ratio
1	AITC	6.42	1879386	0.0000
2	ATC	8.11	153031	0.0000
3	n-hexadecane	11.06	346016	0.0000
			2388432	0.0000

Figure 7: Chromatogram of a 153.7 mg in 10 mL AITC Technical, batch QJH120312 test item solution

11.3 ^{1}H-NMR Spectroscopy



AITC



ATC

Figure 8: Scheme of AITC and ATC stuctures for ^{1}H-NMR signal assignment

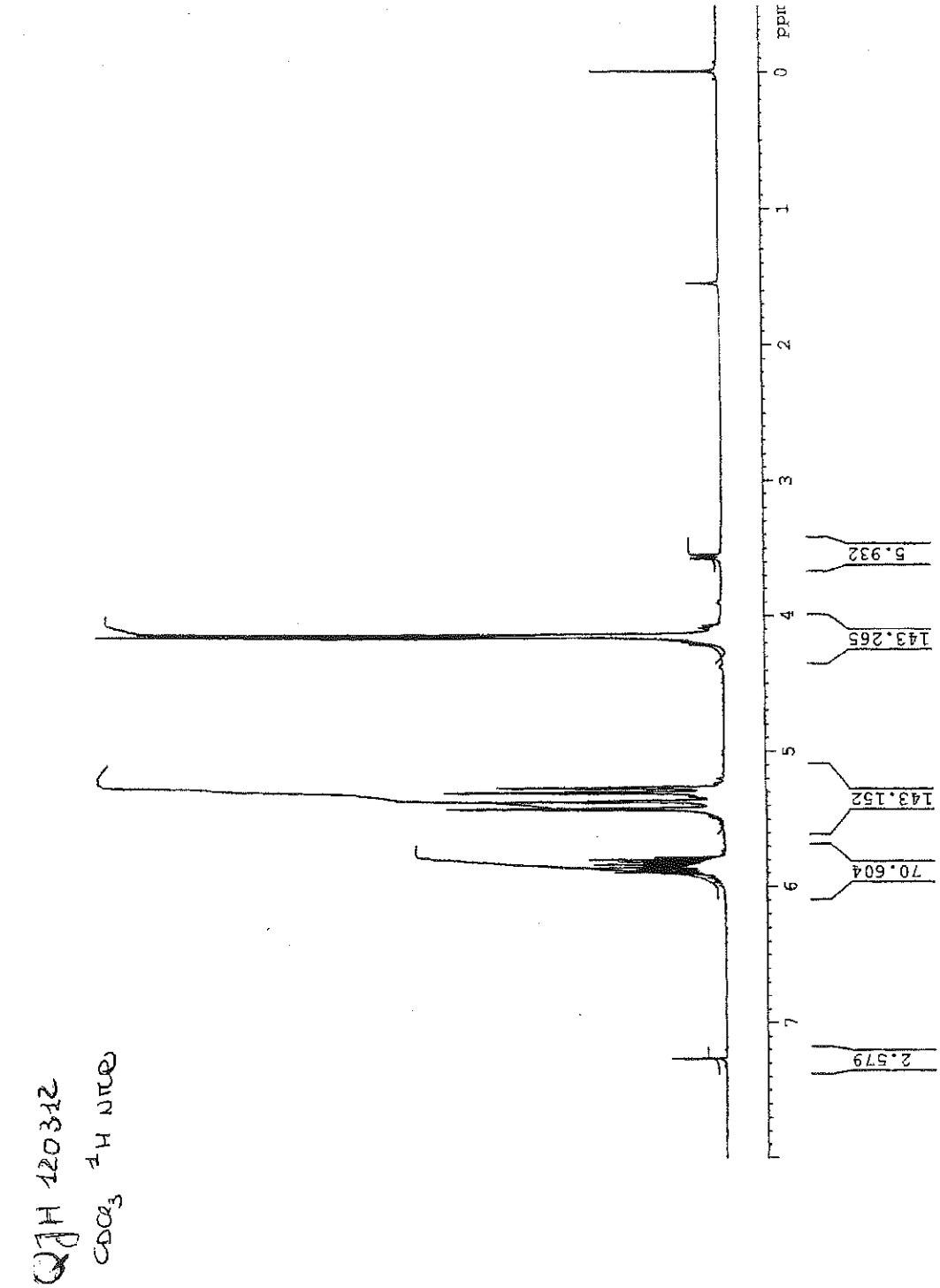


Figure 9: ^{1}H-NMR spectrum of AITC Technical, batch QJH120312

11.4 Analytical Certificate(s)

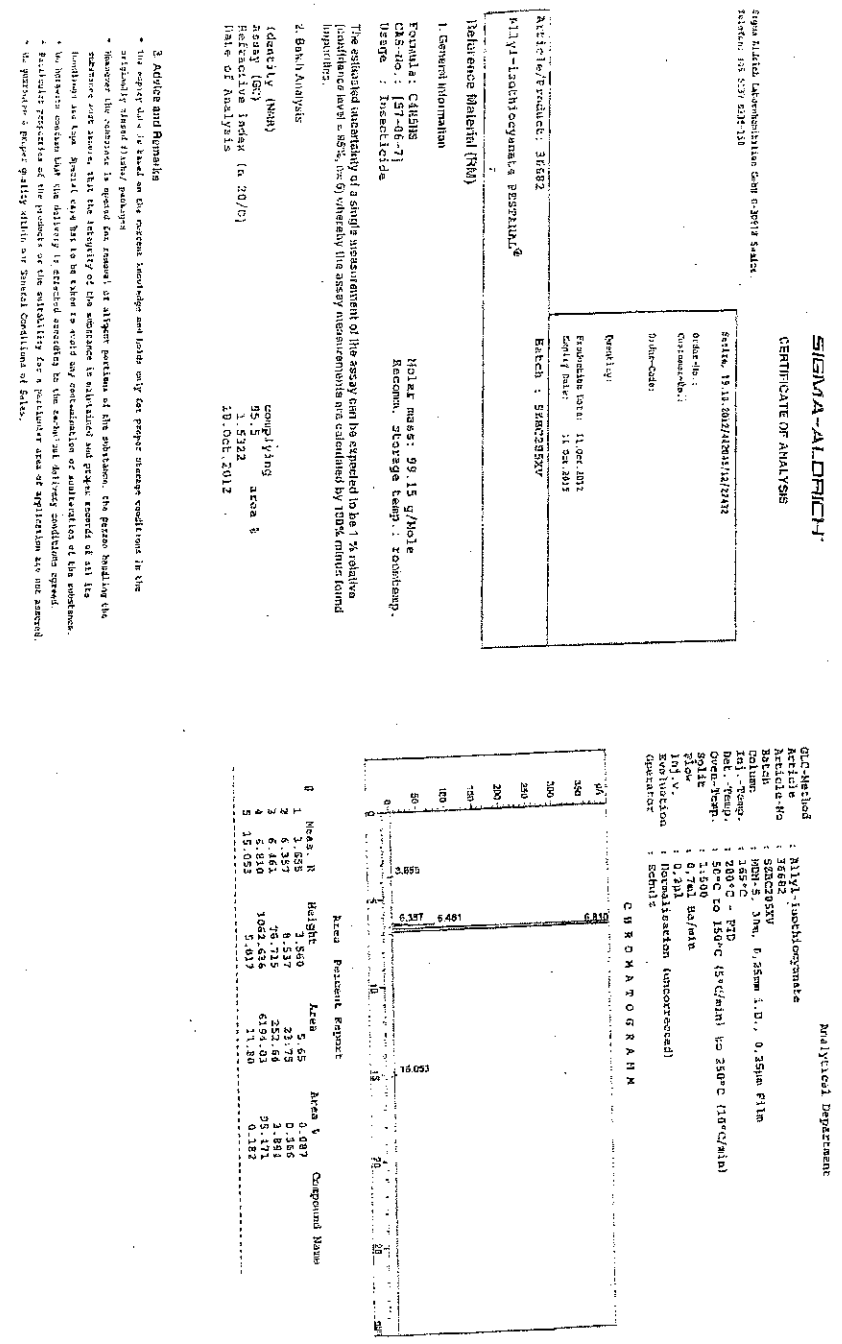


Figure 10: Certificate of analysis of Allyl Isothiocyanate reference item batch SZBC285XV

CERTIFICATE OF ANALYSIS No. 016/12

Sponsor:	ISAGRO S.p.A.
Test Item:	**Allyl Isothiocyanate (AITC) Technical**
Batch Number:	QJH120312
CAS No. (of a.i.):	57-06-7
Sample received on:	26 September 2012
Analysis completion date:	27 November 2012
Expiry date:	November 2014
Method(s):	GC/FID method MA CCF 141-1 described in the GLP Study 12070-01C for purity ^{1}H-NMR spectroscopy for isomers ratio at ambient temperature

Purity (as sum of AITC and ATC ismoers)	**100.5 ± 1.2 % w/w RSD % = 1.22**
AITC/ATC ratio (at ambient temperature)	**96:4**

Poggio Renatico, 21 December 2012

Dr. Sara Morsiani
Study Director

Dr. Kimema Nyatemi
Quality Assurance

Figure 11: Certificate of analysis of Allyl Isothiocyanate (AITC) Technical, batch QJH120312

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6.3 APPENDIX C: Certificate of analysis of AITC of natural origin and comparative HPLC analyses

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RenoLAB GLP

GLP compliant facility

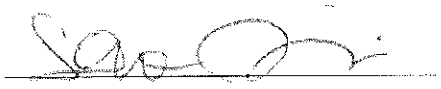
Renolab S.r.l.
Via A. Spinelli, 12 I-44028 Poggio Renatico (Ferrara) Italy
Phone : +39 0532 82 11 16 Fax : +39 0532 82 40 91

CERTIFICATE OF ANALYSIS No. 004/13

Sponsor:	ISAGRO S.p.A. Centro Uffici San Siro, Edificio D-ala 3 Via Caldera 21, I-20153 Milano (MI), Italy
Test Item:	**Allyl Isothiocyanate (AITC) Technical of natural origin**
Batch number:	1050120806/11
CAS No. (of a.i.):	57-06-7 Allyl isothiocyanate (AITC) or oil of mustard
Physical state:	Limpid orange liquid
Molecular Weight	99.15 g/mol
Renolab Study	**2013-05NC**
Sample received on:	15 January 2013
Analysis completion date:	21 February 2013
Expiry date:	February 2015
Type of assay:	GC analysis with FID detection

Determination	Result	Method
Density [g/mL]	1.016	CIPAC MT 3.2.1 (Pyknometer method)
a.i. content as sum of AITC/ATC isomers [% w/w]	98.93 % (98.93 – 98.93 – 98.93)	GC-FID internal method
a.i. content [g/L]	1005	

Analyst: Dr. Sara Morsiani



Poggio Renatico, 21 February 2013

Comparison between Allyl Isothiocyanate Technical of natural origin and Allyl Isothiocyanate Technical from synthesis

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Sample Name	: DCM	Data Acquisition Time	: 10/4/2012 5:01:10 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/1	Operator	: LG
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 1		

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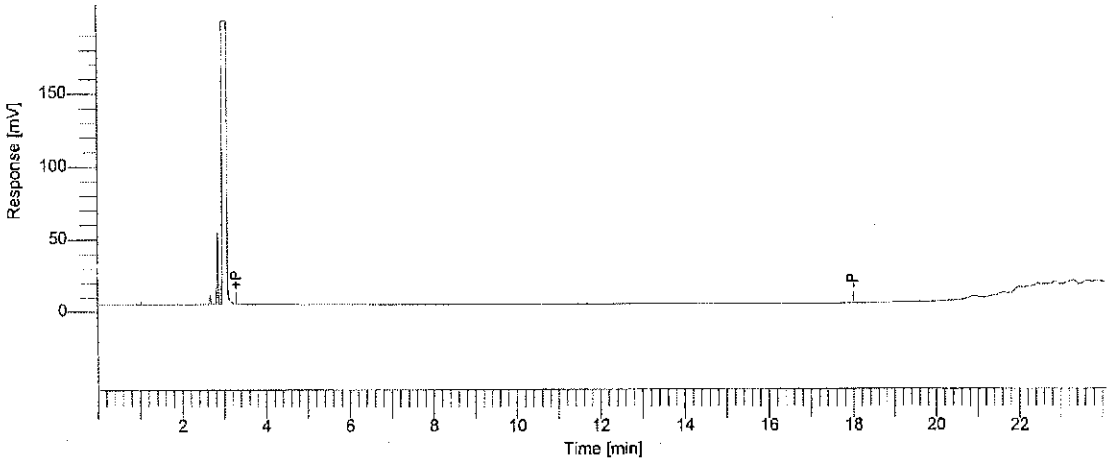

Figure 1: Chromatogram of a dichloromethane (DCM) solvent injection

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Sample Name	: AITC 15 mg/mL in DCM	Data Acquisition Time	: 10/4/2012 6:04:59 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/2	Operator	: LG
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 1		

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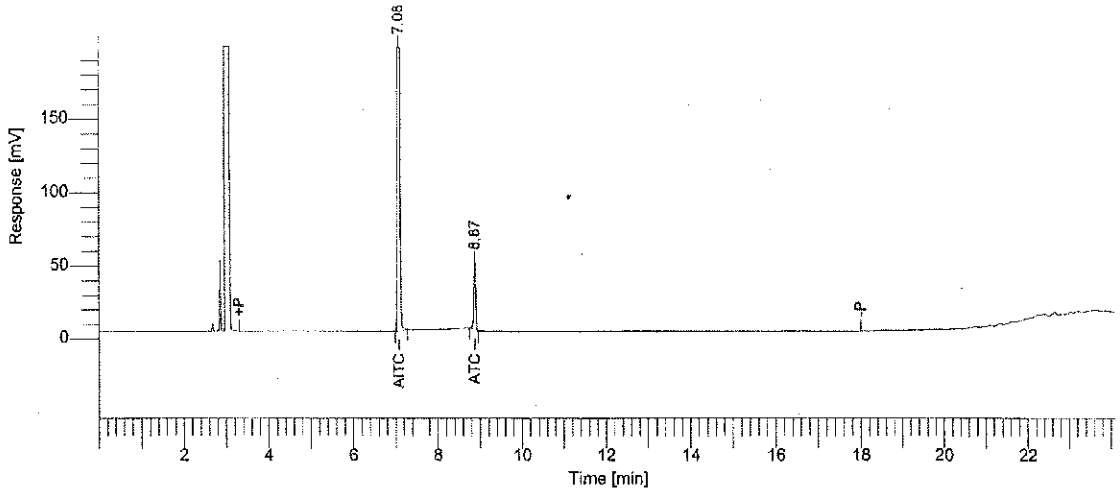

Allyl Isothiocyanate Purity

Peak #	Component Name	Time [min]	Area [uV*sec]	Area [%]
1	AITC	7.08	1960780	93.30
2	ATC	8.87	140785	6.70
			2101566	100.00

Figure 2: Chromatogram of a 15.0 mg/mL Allyl Isothiocyanate Technical from synthesis, batch QJH120312, test item solution.

Software Version	: 6.2.1.0.104:0104	Date	: 2/25/2013 4:29:57 PM
Sample Name	: Sample 1 (1)	Data Acquisition Time	: 2/20/2013 12:59:07 PM
Instrument Name	: AutosystemXL	Channel	: A
Rack/Vial	: 0/2	Operator	: lg
Sample Amount	: 1.000000	Dilution Factor	: 1.000000
Cycle	: 1		

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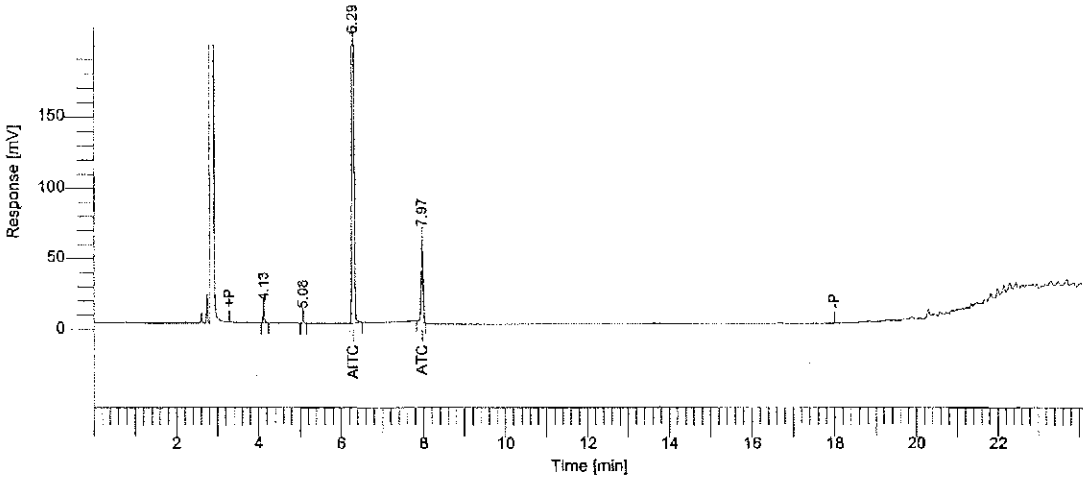

Allyl Isothiocyanate Purity

Peak #	Component Name	Time [min]	Area [uV*sec]	Area [%]
1		4.13	18132	0.84
2		5.08	4917	0.23
3	AITC	6.29	1941756	90.37
4	ATC	7.97	183891	8.56
			2148696	100.00

Figure 3: Chromatogram of a 14.8 mg/mL Allyl Isothiocyanate Technical of natural origin, batch 1050120806/11, test item solution.

Date 25 FEB 2013

6.4 APPENDIX D: GC/MS analysis of the samples of synthetic and natural origin

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AITC – GC-MS analysis

The following samples of Allylisothiocyanate (AITC) were analysed by GC-MS.

1.
AITC of *synthetic* origin
Batch: **QJH1203012**

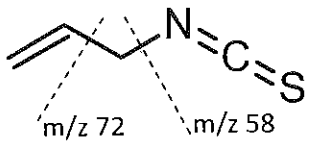
2.
AITC of *natural* origin
Sample name: **"Mostarda OE"**
Batch: **1050120806/11**

The scope of the analysis was to confirm the identity of the active ingredient in each sample through identification of characteristic molecular ion peak and fragmentation.

Test conditions

Instrument:	Agilent Technologies Gaschromatograph 7890A
Detector:	Agilent Technologies 5975C electron impact, single quadrupole
Capillary column:	HP-5; l. 30 m; i.d. 0.32 mm; f.t. 0.25 µm
Carrier gas:	Helium, 1.0 mL/min
Injector temperature:	270 °C
Temperature program:	50°C – 3 min – 12°C/min – 300°C
Sample preparation:	ca. 17.5 mg/mL substance dissolved in dichloromethane
Injected volume:	1 µL
Retention times:	5.7 min (AITC) 5.4 min (ATC)

Fragmentation:



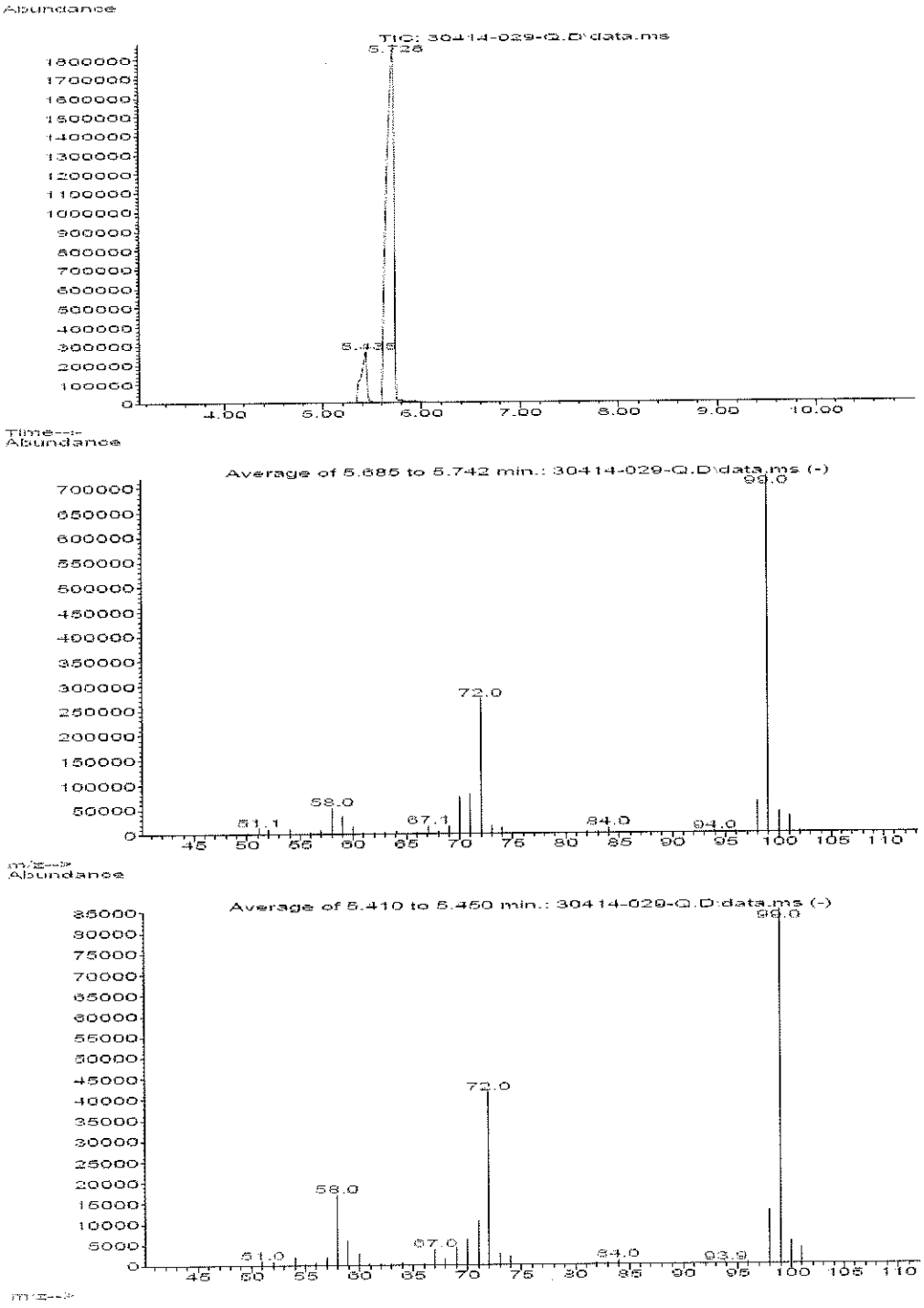
Conclusions:

- ***The current AITC samples of synthetic and natural origin both display mass spectra in agreement with expected molecular ion peak (M^+, m/z 99) and fragmentation.***
- ***In the particular gaschromatographic conditions, each product appears as a mixture of isomers, due to the presence of Allylthiocyanate (ATC) as a secondary peak.***

Annexes:

1. Chromatogram; mass spectrum (AITC); mass spectrum (ATC) for sample QJH1203012 (synthetic origin).
2. Chromatogram; mass spectrum (AITC); mass spectrum (ATC) for sample 1050120806/11 (natural origin).

Ann. 1.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m/z-->
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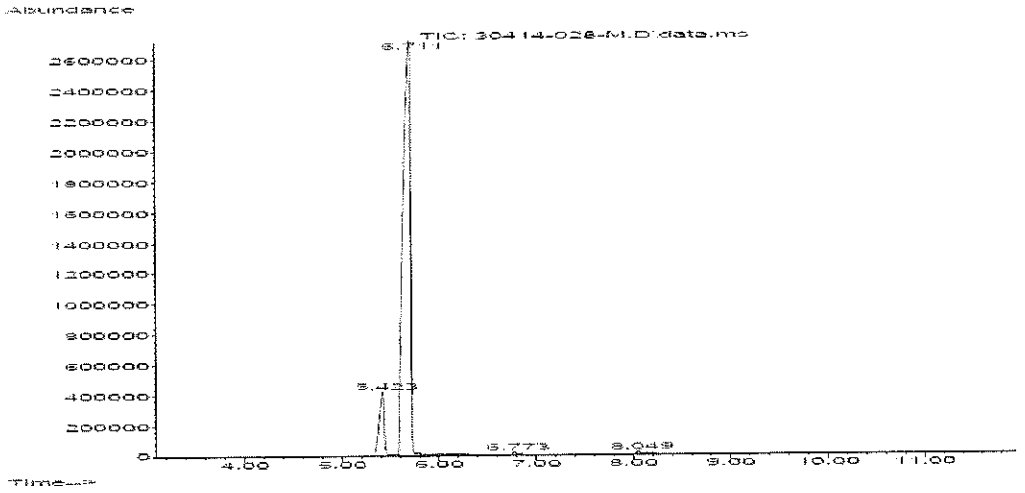
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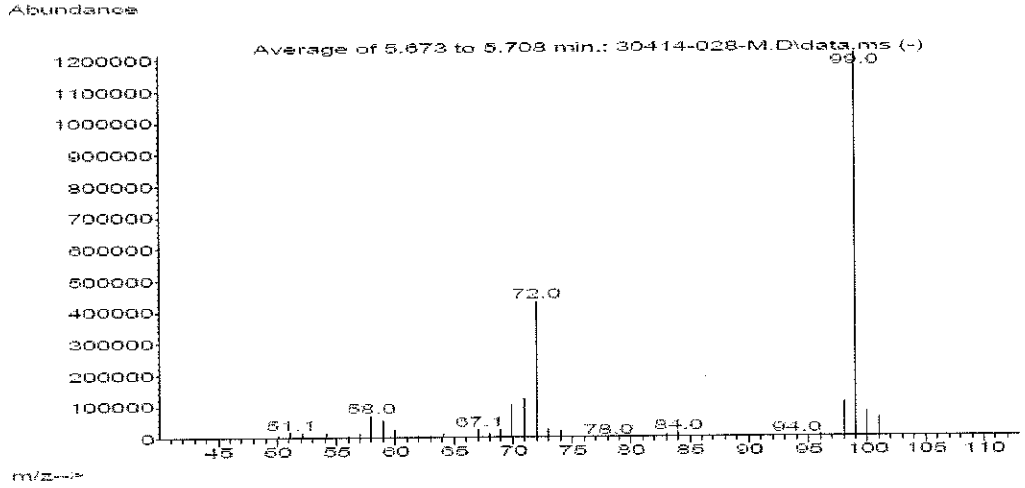
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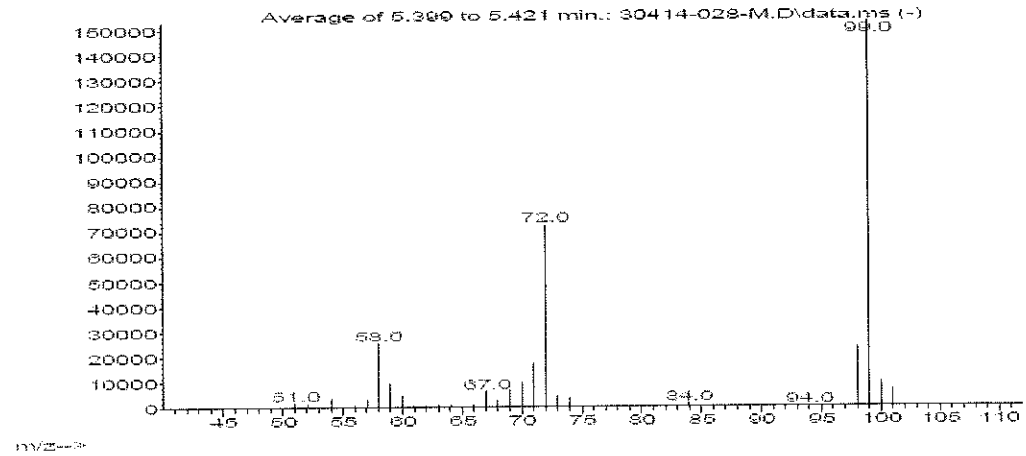
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58.0
51.0
67.0
84.0
94.0
m/z-->

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6.5 APPENDIX E: ^{1}H-NMR analysis of the samples of synthetic and natural origin

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AITC – ^{1}HNMR analysis

The following samples of Allylisothiocyanate (AITC), comprising the isomer Allylthiocyanate (ATC) were analysed by means of proton magnetic resonance; and related spectra were recorded.

1.
AITC of *synthetic* origin
Batch: **QJH1203012**

2.
AITC of *natural* origin
Sample name: **"Mostarda OE"**
Batch: **1050120806/11**

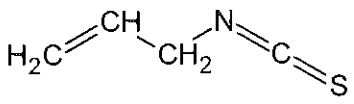
The scope of the analysis were:

a. to confirm the identity of the active ingredient in each sample through identification and integration of characteristic resonance peaks;
b. to determine the AITC/ATC ratio from integration of relative area of specific NMR signals.

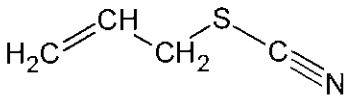
Test conditions

Instrument:	Bruker HNMR 30 MHz
Sample preparation:	ca. 20 mg/mL substance dissolved in deuterated chloroform.

The peak integration of $-CH_2-$ groups was adopted as the measure for the AITC/ATC relative abundance in each sample.
The relevant NMR signals (doublets) for the $-CH_2-$ groups are found respectively at 4.17 ppm (in AITC) and at 3.55 ppm (in ATC).
Other signals in the NMR graphs are at 5.2 – 5.5 ppm ($=CH_2$) and 5.8 – 6.0 ppm (=CH-); attribution to AITC or ATC is not applicable.



AITC



ATC

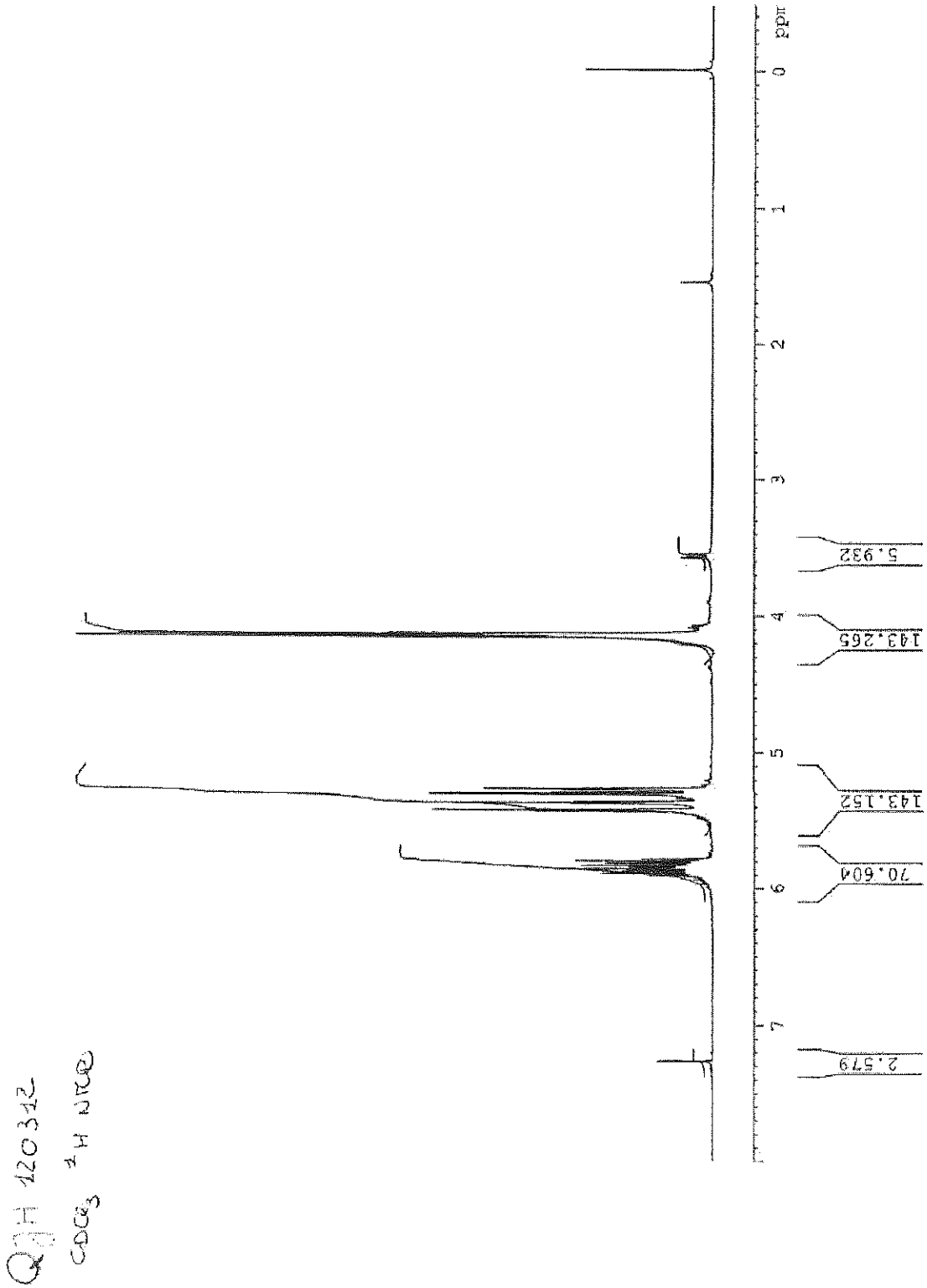
Conclusions:

- ***The current AITC samples of synthetic and natural origin both result composed of 96% AITC and 4% ATC, in relative abundance.***

Annexes:

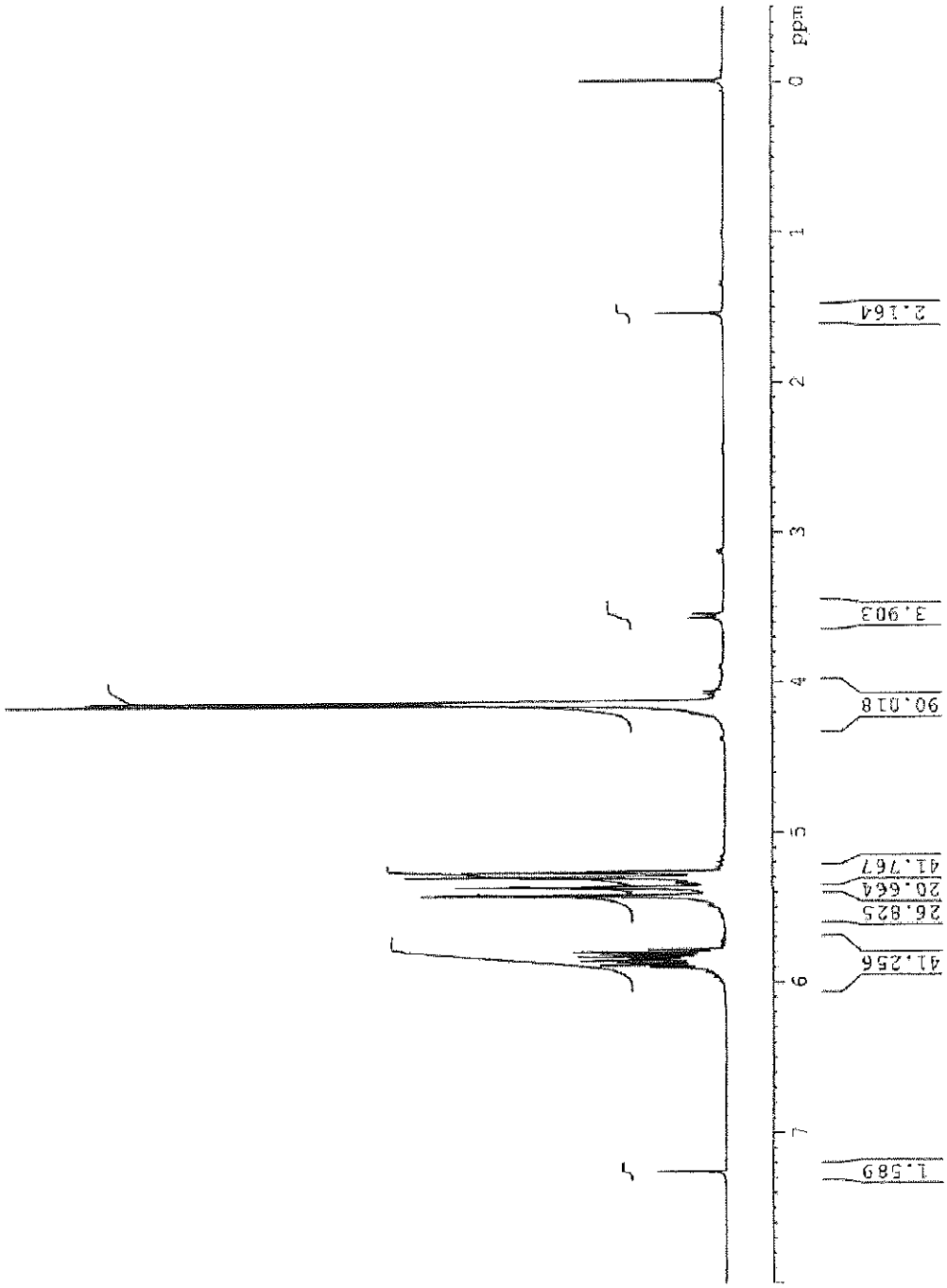
1. ^{1}HNMR graph for sample QJH1203012 (synthetic origin).
2. ^{1}HNMR graph for sample 1050120806/11 (natural origin).

Ann.1



QTH 120312
$CDCl_3$ ^1H NMR

Ann.2



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6.6 APPENDIX F: Physical-chemical characterisation of AITC of synthetic origin

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Final Report

Physical-Chemical Characterisation of a Sample of AITC Technical

Guideline(s)

OECD guidelines and US EPA/OPPTS series 830

Study Director

Dr. Lidia Gazzotti

Date

22 February 2013

Test Facility

Renolab S.r.l.
Via Spinelli, 12
I-44028 Poggio Renatico (FE)
Italy

Sponsor

ISAGRO S.p.A.
Centro Uffici San Siro Edificio D – ala 3
Via Caldera, 21
I-20153 Milano (MI)
Italy

Test item

AITC Technical

Study code

12070-02C

Statement of Confidentiality

This report contains confidential and proprietary information of ISAGRO S.p.A. which must not be disclosed to anyone except the employees of this company or to persons authorised by law or judicial judgement without the expressed and written approval of ISAGRO S.p.A.

Statement of Compliance with the Principles of Good Laboratory Practice

The study described in this report was conducted in compliance with the most recent edition of:

- Law Decree 2nd March 2007 N° 50 – Actuation of Directives 2004/9/EC and 2004/10/EC concerning the inspection and verification of Good Laboratory Practice (GLP) and aligning of laws, regulations and administrative provisions related to the application of the Principles of Good Laboratory Practice and to the control of their application for chemicals tests.
- The OECD Principles of Good Laboratory Practice.

The Italian requirements are based on the OECD Principles of Good Laboratory Practice which are accepted by regulatory authorities throughout the European Community, the United States of America (FDA and EPA) and Japan (MHW, MAFF and METI) on the basis of intergovernmental agreements.

This report fully and accurately reflects the procedure used and data generated.

Dr. Lidia Gazzotti
Study Director

22 FEB 2013
Date

Statement of Quality Assurance Unit

Study code:	12070-02C
Study title:	Physical-Chemical Characterisation of AITC Technical

Study plan has been verified and experimental phase, draft report and final report of this study were audited by the Quality Assurance in compliance with the OECD Guidelines and to Renolab's Standard Operating Procedures Audit dates are given below:

Phase or document	Date of verification /audit	Date of report to			
		Principal Investigator	Test site Management	Study Director	Test Facility Management
Study plan:	24 JAN 2013	n.a.	n.a.	n.a.	n.a.
Experimental analytical phase	30 JAN 2013	n.a.	n.a.	01 FEB 2013	04 FEB 2013
Draft Final report:	22 FEB 2013	n.a.	n.a.	22 FEB 2013	22 FEB 2013

The draft report correspond to the raw data.

P. Bonetti

Dr. Paolo Bonetti
Quality Assurance

22 FEB 2013

Date

Index

List of tables

List of Figures

1 Summary

The following physical-chemical characteristics of AITC technical batch QJH120312 were determined.

Test	Method	Result			
Boiling Point	OECD 103	420 K (147°C)			
Density/Relative Density	CIPAC 3.2	1.017 g/mL			
UV/visible absorption spectra	OECD 101	Type of phase and pH	Observed λ_{max} (nm)	Absorbance (AU)	Calculated ε ($M^{-1}cm^{-1}$)
		Methanol pH 1.81	203	1.6130	3877
		Methanol pH 6.61	203	1.2328	2701
		Methanol pH 11.29	203	1.2738	2618
		Methanol pH 1.81	245	0.6320	1519
		Methanol pH 6.61	246	0.4486	983
		Methanol pH 11.29	246	0.4243	872

2 Time Schedule

Study plan authorisation:	24 January 2013
Start of experimental phase:	30 January 2013
End of experimental phase:	01 February 2013
Draft report:	01 February 2013
Study completion date	22 February 2013

3 Study Objective

The aim of this study is the determination of density, boiling point and UV spectra of Allyl Isothiocyanate (AITC) Technical.

4 Materials

4.1 Test item

Name:	Allyl Isothiocyanate (AITC) Technical
Active ingredient(s) (common name and synonym)	Allyl Isothiocyanate (AITC) or oil of mustard
Active ingredient(s) IUPAC name:	3-isothiocyanatoprop-1-ene
CAS Number of a.i.(s):	57-06-7
Physical state:	Limpid orange liquid
Molecular Weight	99.15 g/mol
Supplier:	ISAGRO RICERCA S.r.l.
Batch number:	QJH120312
Renolab Code:	12070
Expiry date:	September 2014
Storage conditions:	Room temperature

4.2 Apparatus

- Apparatus for melting/boiling point, Büchi
- Standard laboratory glassware and equipment
- Analytical balance accurate to 0.1 mg, Mettler-Toledo
- pH-meter, mod. 827 pH lab Metrohm
- Thermostatic bath with immersion thermostat, Haake
- UV/Visible spectroscopy system, Agilent

4.3 Reagents

- Hydrochloric acid solution 0.1M, Carlo Erba
- Sodium hydroxide solution 0.1M, Carlo Erba
- Methanol gradient grade, Sigma Aldrich

5 Physical-Chemical Characterisations

5.1 Boiling point (OECD 103)

The boiling point is defined as the temperature at which the phase transition from the liquid to the gas state at atmospheric pressure takes place.

5.1.1 Outline of method(s)

Boiling point was determined by the Siwoboloff method, placing the substance in a capillary immersed in a liquid bath method over the temperature range ambient to 593 K (320 °C).

A portion of the test item was put in a tube which was immersed in a liquid bath. The apparatus and then the stirrer motor, the heating circuit and the lamp to illuminate the sample, were switched on and the sample is gradually heated. The sample tube was held in close contact with a thermometer and it contains a boiling capillary which is fused about 1 cm above its lower end. The bath was heated at a rate of about 3 K per minutes to about 10 degrees below the expected boiling point, then the

current was reduced to 1 K per minute. Upon approach of the boiling temperature bubbles emerge rapidly from the lower open end of the capillary. The boiling temperature is that temperature at which, on momentary cooling, the string of bubbles stops and liquid suddenly rises in the capillary. The test was performed in triplicate assay.

5.1.2 Calculations

The measured temperature was converted from °C to K using the following equation:

$$T = t + 273$$

where:

T: temperature in Kelvin degrees

t: temperature in Celsius degrees

5.1.3 Result of boiling point

The results of the boiling point determinations were reported in Table 1.

Table 1: Results of AITC Technical boiling point determination

Boiling point		
	Temperature	
	°C	K
Determination 1	147	420
Determination 2	146	419
Determination 3	147	420
Mean	**147**	**420**

5.2 Density (CIPAC MT 3.2)

The 25 mL pycnometer (including the rids) was weighted empty, then filled with water and incubated for at least 15 min at 20 °C (water bath, calibrated thermometer). The surface of the pycnometer was dried and the pycnometer was weighed.

After cleaning and drying, the pycnometer was filled with the test item sonicated in order to degas and incubated for at least 15 min at 20 °C as above.

The test was conducted at the temperature of 20 °C.

5.2.1 Calculation

The density was calculated from the following equation:

$$\rho = \frac{(w_3 - w_2)}{(w_1 - w_0)} \cdot \rho_{H2O}$$

ρ Density of test substance (g/mL)

m_0 Mass of empty pycnometer before measure with water(g)

m_1 Mass of pycnometer filled with water (g)

m_2 Mass of empty pycnometer before measure with test item (g)

m_3 Mass of pycnometer filled with test item (g)

ρ_{H2O} Density of water (0.9982 g/mL at 20 °C)

5.2.2 Results

Table 2: Results for density determination

Determination	Density at 20°C (g/mL)
1	1.017
2	1.017
Mean value	**1.017**

5.3 UV/Visible absorption spectra (OECD 101)

The ultraviolet-visible (UV-VIS) absorption spectrum of a chemical compound gives some indication of the wavelengths at which the compound may be susceptible to photochemical degradation.

5.3.1 Outline of method(s)

The absorption of a compound is due to its particular chemical form. It is often the case that different forms are present, depending on whether the medium is acidic, basic or neutral. Consequently, spectra under all three conditions are required where solubility and concentration allow. Where it was not possible to obtain sufficient concentrations in any of the aqueous media, a suitable organic solvent was used (methanol preferred). The acid medium should have a pH of less than 2, and the basic medium should be at least pH 10.

Test item solutions were prepared by accurately weighting about 15 mg of the test substance in a 20 mL volumetric flask and making up to volume with the tested phase. The test item solution was diluted 20 times in order to achieve a concentration that produced at least one absorbance maximum in the range 0.5 to 1.5 units.

UV/Visible absorption spectra were acquired by a single beam UV/visible spectroscopy system over the wavelength range 1900-750 nm at 1-nm intervals with a 1 cm cell path length.

5.3.2 Calculations

The molar absorption coefficient ε was calculated as follows for all the maximum absorbance value of the test item.

$$\varepsilon_{\lambda}\ (M^{-1}cm^{-1}) = \frac{A}{C \times d}$$

λ wavelength (nm) of the observed maximum

A observed absorbance of maximum

C test substance concentration (M)

d cell path length (1 cm)

5.3.3 Reagents solutions preparation

Due to the hydrophobic nature of the test item methanol was used as solvent instead of pure water. Acid and basic pHs were achieved by adding respectively HCl 0.1 M and NaOH 0.1 M to 100 mL of solvent until reaching pH 1.81 and 11.29.

5.3.4 Results

Two peaks were found in the UV range, molar extinction coefficient was calculated at both wavelengths.

Table 3: Table of result of AITC Technical spectra

Medium	Maximum wavelength (nm)	Absorbance (AU)	Sample Conc (M)	ε ($M^{-1}cm^{-1}$)
pH 1.81	203	1.6130	4.1604E-04	3877
pH 6.61	203	1.2328	4.5638E-04	2701
pH 11.29	203	1.2738	4.8664E-04	2618
pH 1.81	245	0.6320	4.1604E-04	1519
pH 6.61	246	0.4486	4.5638E-04	983
pH 11.29	246	0.4243	4.8664E-04	872

Representatives spectra are shown in figure from 1 to 3 in Appendices

All the data reported in the tables of this report are rounded values taken from Excel spreadsheets which will be archived with the raw data. The use of Excel spreadsheets to make the calculations produces more accurate endpoints. These endpoints may occasionally slightly differ from the values derived by substituting the rounded values in calculations.

6 Amendments/Deviations

The study was performed according to Study Plan 12070-02C dated 24 January. This report reflects the conduct of this study.

7 Archiving

For the periods demanded by the principles of GLP the following documents and materials will be archived:

- Study plan, raw data, and the final report (10 years).
- All documentation generated by the Quality Assurance Unit (10 years).
- A sample of the test item (1 year) and reference item.

All documents and materials will be stored in the archives of Renolab S.r.l. The premises for storing the documents and materials are settled according to the principles of Good Laboratory Practice in the organization of the testing facility.

8 Reference (s)

OECD guidelines for testing of chemicalsNo. 101; 103 and 109

EPA/OPPTS Series 830 guidelines

CIPAC Handbook Vol. F Physico-chemicals Methods for Technical and Formulated Pesticides, W. Dobrat and A. Martijn Editors, (1995)

9 Distribution

	Study Plan	Raw Data	Final Report
Sponsor:	1 original	-	1 original
Test Facility:	1 original	1 original	1 original + 1 pdf file

10 Appendices: Spectra

Spectrum/Peak Report Date 02/01/2013 Time 09:11:54 Page 1 of 1

Method file : ALLYL.M Last update: Date 01/29/2013 Time 6:04:03 PM
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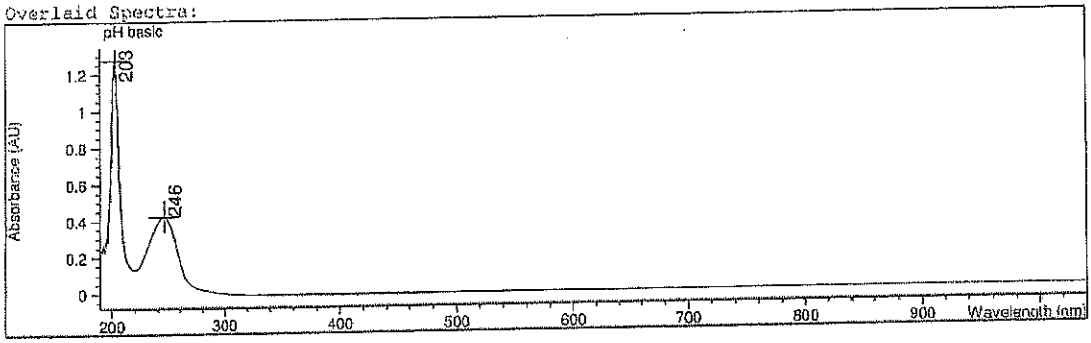

#	Name	Peaks (nm)	Abs (AU)	#	Name	Peaks (nm)	Abs (AU)
1	pH basic	203.0	1.27860	1		246.0	0.42397

Report generated by : ML Signature: .....

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Figure 1: Spectrum at basic condition in UV/Vis spectra determination

Spectrum/Peak Report Date 02/01/2013 Time 09:32:50 Page 1 of 1

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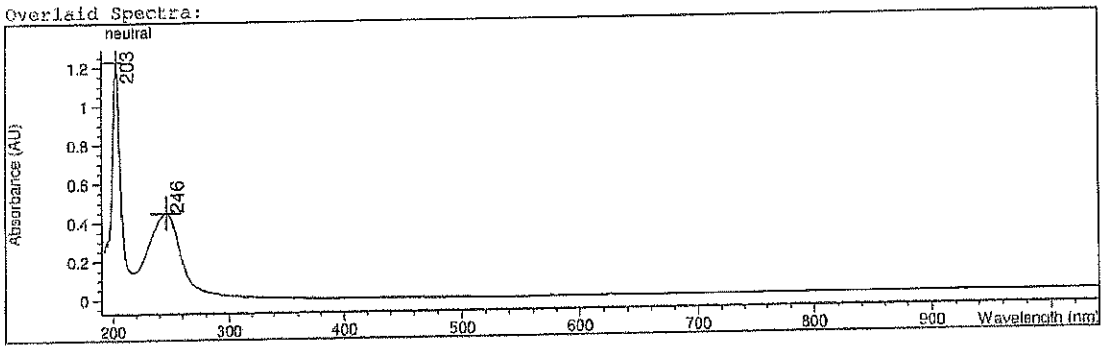

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1	neutral	203.0	1.22930	1		246.0	0.44848

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Figure 2: Spectrum at neutral condition in UV/Vis spectra determination

Spectrum/Peak Report Date 02/01/2013 Time 09:13:25 Page 1 of 1

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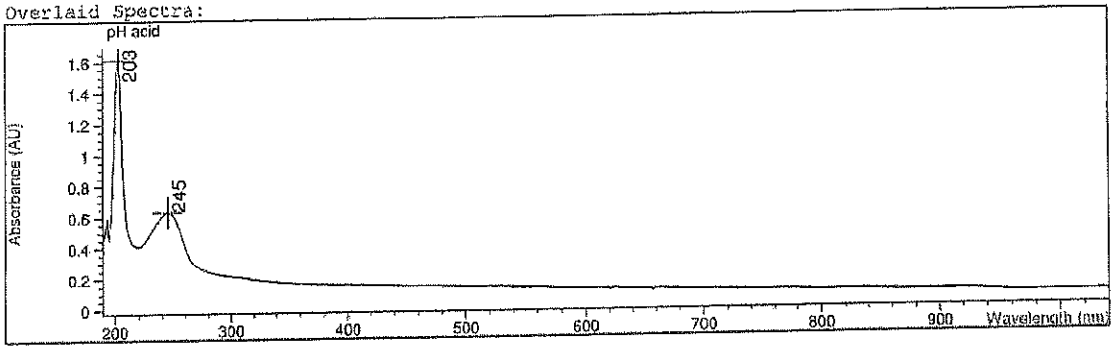

#	Name	Peaks(nm)	Abs(AU)	#	Name	Peaks(nm)	Abs(AU)
1	pH acid	203.0	1.61580	1		245.0	0.63243

Report generated by : ML Signature: .....

*** End Spectrum/Peak Report ***

Figure 3: Spectrum at acid condition in UV/Vis spectra determination

6.7 APPENDIX G: Physical-chemical characterisation of AITC of natural origin

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Final Report

Physical-Chemical Characterisation of a Sample of AITC Technical of natural origin

Guideline(s)

OECD guidelines and US EPA/OPPTS series 830

Study Director

Dr. Lidia Gazzotti

Date

22 February 2013

Test Facility

Renolab S.r.l.
Via Spinelli, 12
I-44028 Poggio Renatico (FE)
Italy

Sponsor

ISAGRO S.p.A.
Centro Uffici San Siro Edificio D – ala 3
Via Caldera, 21
I-20153 Milano (MI)
Italy

Test item

AITC Technical

Study code

13002-01C

Statement of Confidentiality

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Statement of Compliance with the Principles of Good Laboratory Practice

The study described in this report was conducted in compliance with the most recent edition of:

- Law Decree 2nd March 2007 N° 50 – Actuation of Directives 2004/9/EC and 2004/10/EC concerning the inspection and verification of Good Laboratory Practice (GLP) and aligning of laws, regulations and administrative provisions related to the application of the Principles of Good Laboratory Practice and to the control of their application for chemicals tests.
- The OECD Principles of Good Laboratory Practice.

The Italian requirements are based on the OECD Principles of Good Laboratory Practice which are accepted by regulatory authorities throughout the European Community, the United States of America (FDA and EPA) and Japan (MHW, MAFF and METI) on the basis of intergovernmental agreements.

This report fully and accurately reflects the procedure used and data generated.

Dr. Lidia Gazzotti
Study Director

22 FEB 2013
Date

Statement of Quality Assurance Unit

Study code:	13002-01C
Study title:	Physical-Chemical Characterisation of AITC Technical

Study plan has been verified and experimental phase, draft report and final report of this study were audited by the Quality Assurance in compliance with the OECD Guidelines and to Renolab's Standard Operating Procedures Audit dates are given below:

Phase or document	Date of verification /audit	Date of report to			
		Principal Investigator	Test site Management	Study Director	Test Facility Management
Study plan:	24 JAN 2013	n.a.	n.a.	n.a.	n.a.
Experimental analytical phase	30 JAN 2013	n.a.	n.a.	01 FEB 2013	04 FEB 2013
Draft Final report:	21 FEB 2013	n.a.	n.a.	22 FEB 2013	22 FEB 2013

The draft report corresponds to the raw data.

P. Bonetti

Dr. Paola Bonetti
Quality Assurance

22 FEB 2013
Date

Index

List of tables

List of Figures

1 Summary

The following physical-chemical characteristics of AITC technical of natural origin batch 1050120806/11 were determined.

Test	Method	Result			
Boiling Point	OECD 103	422 K (149°C)			
Density/Relative Density	CIPAC 3.2	1.016 g/mL			
UV/visible absorption spectra	OECD 101	Type of phase and pH	Observed λ_{max} (nm)	Absorbance (AU)	Calculated ε ($M^{-1}cm^{-1}$)
		Methanol pH 1.81	202	1.2124	2968
		Methanol pH 6.61	203	1.3277	3116
		Methanol pH 11.29	203	1.2370	2820
		Methanol pH 1.81	245	0.3187	748
		Methanol pH 6.61	246	0.4743	1161
		Methanol pH 11.29	244	0.4415	1006

2 Time Schedule

Study plan authorisation:	24 January 2013
Start of experimental phase:	30 January 2013
End of experimental phase:	01 February 2013
Draft report:	01 February 2013
Study completion date	22 February 2013

3 Study Objective

The aim of this study is the determination of density, boiling point and UV spectra of Allyl Isothiocyanate (AITC) Technical of natural origin.

4 Materials

4.1 Test item

Name:	Allyl Isothiocyanate (AITC) Technical of natural origin
Active ingredient(s) (common name and synonym)	Allyl Isothiocyanate (AITC) or oil of mustard
Active ingredient(s) IUPAC name:	3-isothiocyanatoprop-1-ene
CAS Number of a.i.(s):	57-06-7
Physical state:	Limpid orange liquid
Molecular Weight	99.15 g/mol
Supplier:	ISAGRO RICERCA S.r.l.
Batch number:	1050120806/11
Renolab Code:	13002
Expiry date:	Jul 2014
Storage conditions:	Room temperature

4.2 Apparatus

- Apparatus for melting/boiling point, Büchi
- Standard laboratory glassware and equipment
- pH-meter, mod. 827 pH lab Metrohm
- Spectrophotometer UV/Visible, Agilent mod. 8453
- Thermostatic bath with immersion thermostat, Haake mod. DC3
- Analytical balance accurate to 0.1 mg, Mettler-Toledo mod. AT261

4.3 Reagents

- Hydrochloric acid solution 0.1M, Carlo Erba
- Sodium hydroxide solution 0.1M, Carlo Erba
- Methanol gradient grade, Sigma Aldrich

5 Physical-Chemical Characterisations

5.1 Boiling point (OECD 103)

The boiling point is defined as the temperature at which the phase transition from the liquid to the gas state at atmospheric pressure takes place.

5.1.1 Outline of method(s)

Boiling point was determined by the Siwoboloff method, placing the substance in a capillary immersed in a liquid bath method over the temperature range ambient to 593 K (320 °C).

A portion of the test item was put in a tube which was immersed in a liquid bath. The apparatus and then the stirrer motor, the heating circuit and the lamp to illuminate the sample, were switched on and the sample is gradually heated. The sample tube was held in close contact with a thermometer and it contains a boiling capillary which is fused about 1 cm above its lower end. The bath was heated at a rate of about 3 K per minutes to about 10 degrees below the expected boiling point, then the

current was reduced to 1 K per minute. Upon approach of the boiling temperature bubbles emerge rapidly from the lower open end of the capillary. The boiling temperature is that temperature at which, on momentary cooling, the string of bubbles stops and liquid suddenly rises in the capillary. The test was performed in tripilcate assay.

5.1.2 Calculations

The measured temperature was converted from °C to K using the following equation:

$$T = t + 273$$

where:

T: temperature in Kelvin degrees

t: temperature in Celsius degrees

5.1.3 Result of boiling point

The results of the boiling point determinations were reported in Table 1.

Table 1: Results of AITC Technical boiling point determination

Boiling point		
	Temperature	
	°C	K
Determination 1	149	422
Determination 2	149	422
Determination 3	150	423
Mean	**149**	**422**

5.2 Density (CIPAC MT 3.2)

The 25 mL pycnometer (including the rids) was weighted empty, then filled with water and incubated for at least 15 min at 20 °C (water bath, calibrated thermometer). The surface of the pycnometer was dried and the pycnometer was weighed.

After cleaning and drying, the pycnometer was filled with the test item sonicated in order to degas and incubated for at least 15 min at 20 °C as above.

The test was conducted at the temperature of 20 °C.

5.2.1 Calculation

The density was calculated from the following equation:

$$\rho = \frac{(w_3 - w_2)}{(w_1 - w_0)} \cdot \rho_{H2O}$$

ρ Density of test substance (g/mL)

m_0 Mass of empty pycnometer before measure with water(g)

m_1 Mass of pycnometer filled with water (g)

m_2 Mass of empty pycnometer before measure with test item (g)

m_3 Mass of pycnometer filled with test item (g)

ρ_{H2O} Density of water (0.9982 g/mL at 20 °C)

5.2.2 Results

Table 2: Results for density determination

Determination	Density at 20°C (g/mL)
1	1.015
2	1.017
Mean value	**1.017**

5.3 UV/Visible absorption spectra (OECD 101)

The ultraviolet-visible (UV-VIS) absorption spectrum of a chemical compound gives some indication of the wavelengths at which the compound may be susceptible to photochemical degradation.

5.3.1 Outline of method(s)

The absorption of a compound is due to its particular chemical form. It is often the case that different forms are present, depending on whether the medium is acidic, basic or neutral. Consequently, spectra under all three conditions are required where solubility and concentration allow. Where it was not possible to obtain sufficient concentrations in any of the aqueous media, a suitable organic solvent was used (methanol preferred). The acid medium should have a pH of less than 2, and the basic medium should be at least pH 10.

Test item solutions were prepared by accurately weighting about 15 mg of the test substance in a 20 mL volumetric flask and making up to volume with the tested phase. The test item solution was diluted 20 times in order to achieve a concentration that produced at least one absorbance maximum in the range 0.5 to 1.5 units.

UV/Visible absorption spectra were acquired by a single beam UV/visible spectroscopy system over the wavelength range 1900-750 nm at 1-nm intervals with a 1 cm cell path length.

5.3.2 Calculations

The molar absorption coefficient ε was calculated as follows for all the maximum absorbance values of the test item.

$$\varepsilon_\lambda\ (M^{-1}cm^{-1}) = \frac{A}{C \times d}$$

λ wavelength (nm) of the observed maximum

A observed absorbance of maximum

C test substance concentration (M)

d cell path length (1 cm)

5.3.3 Reagents solutions preparation

Due to the hydrophobic nature of the test item methanol was used as solvent instead of pure water. Acid and basic pHs were achieved by adding respectively HCl 0.1 M and NaOH 0.1 M to 100 mL of solvent until reaching pH 1.81 and 11.29.

5.3.4 Results

Two peaks were found in the UV range, molar extinction coefficient was calculated at both wavelengths.

Table 3: Table of result of AITC Technical spectra

Medium	Maximum wavelength (nm)	Absorbance (AU)	Sample Conc (M)	ε ($M^{-1}cm^{-1}$)
pH 1.81	202	1.2124	4.0847E-04	2968
pH 6.61	203	1.3277	4.2612E-04	3116
pH 11.29	203	1.2370	4.3873E-04	2820
pH 1.81	245	0.3187	4.2612E-04	748
pH 6.61	246	0.4743	4.0847E-04	1161
pH 11.29	244	0.4415	4.3873E-04	1006

Representatives spectra are shown in figure from 1 to 3 in Appendices

All the data reported in the tables of this report are rounded values taken from Excel spreadsheets which will be archived with the raw data. The use of Excel spreadsheets to make the calculations produces more accurate endpoints. These endpoints may occasionally slightly differ from the values derived by substituting the rounded values in calculations.

6 Amendments/Deviations

The study was performed according to Study Plan 13002-01C dated 24 January. This report reflects the conduct of this study.

7 Archiving

For the periods demanded by the principles of GLP the following documents and materials will be archived:

- Study plan, raw data, and the final report (10 years).
- All documentation generated by the Quality Assurance Unit (10 years).
- A sample of the test item (1 year) and reference item.

All documents and materials will be stored in the archives of Renolab S.r.l. The premises for storing the documents and materials are settled according to the principles of Good Laboratory Practice in the organization of the testing facility.

8 Reference (s)

OECD guidelines for testing of chemicals No. 101; 103 and 109

EPA/OPPTS Series 830 guidelines

CIPAC Handbook Vol. F Physico-chemicals Methods for Technical and Formulated Pesticides, W. Dobrat and A. Martijn Editors, (1995)

9 Distribution

	Study Plan	Raw Data	Final Report
Sponsor:	1 original	-	1 original
Test Facility:	1 original	1 original	1 original + 1 pdf file

10 Appendices: Spectra

Spectrum/Peak Report Date 02/15/2013 Time 18:15:38 Page 1 of 1

Method file : ALLYL.M Last update: Date 01/29/2013 Time 6:04:03 PM
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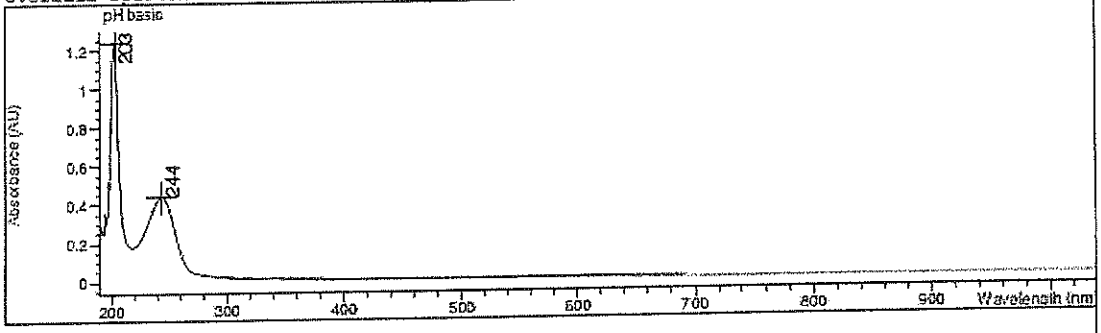

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1	pH basic	203.0	1.23700	1		244.0	0.44159

Report generated by : ML Signature: .....

*** End Spectrum/Peak Report ***

Figure 1: Spectrum at basic condition in UV/Vis spectra determination

Spectrum/Peak Report Date 02/15/2013 Time 18:16:39 Page 1 of 1

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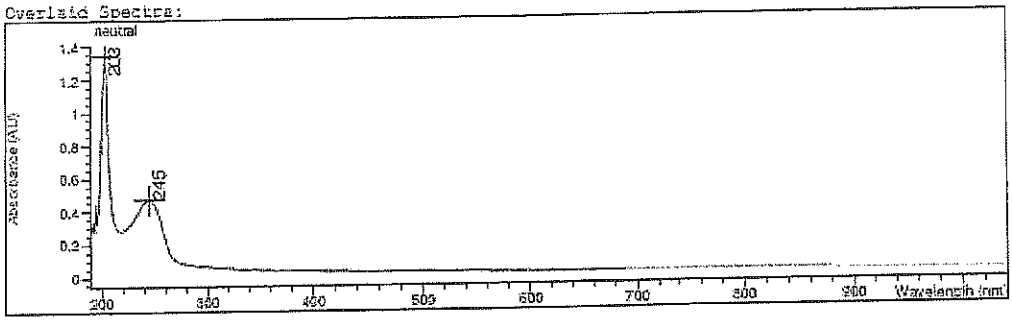

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1	neutral	203.0	1.33890	1		245.0	0.47357

Report generated by : ML Signature: .....

*** End Spectrum/Peak Report ***

Figure 2: Spectrum at neutral condition in UV/Vis spectra determination

Spectrum/Peak Report Date 02/15/2013 Time 18:14:14 Page 1 of 1

Method file : ALLYL.M Last update: Date 01/29/2013 Time 6:04:03 PM
Information : Default Method
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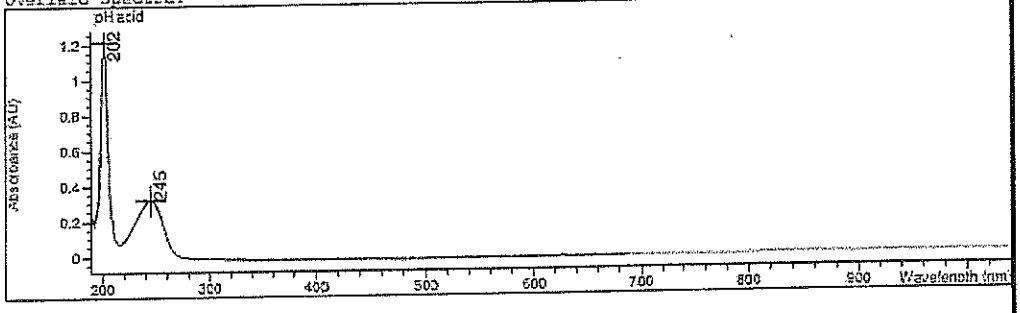

#	Name	Peaks (nm)	Abs (AU)	#	Name	Peaks (nm)	Abs (AU)
1	pH acid	202.0	1.21190	1		245.0	0.31849

Report generated by : ML Signature: .....

*** End Spectrum/Peak Report ***

Figure 3: Spectrum at acid condition in UV/Vis spectra determination

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6.8 APPENDIX H: IR spectroscopy and refractive index of AITC of synthetic origin

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REDOX snc – (Monza) Cert. BPL n°005/2011 Cert. GMP n°053/2012	Sponsor: **Renolab** PAGES IN FULL REPORT: 6	EXTERNAL REPORT NUMBER **050/13** **(Ed.1)**
DEPARTMENT NAME ***Analytical Chemistry & Process Safety Testing Labs***		DATE ISSUED: **19/02/13**

TITLE:

Infrared spectroscopy and refractive index characterization of sample Allyl Isothiocyanate (AITC) (batch QJHI20312)

AUTHOR(S)	PRINCIPAL INVESTIGATOR
M. Calvi 19/2/13 **P. Annoni** 19/02/13	**A. Borriero** 19/02/13

SUMMARY

The sample Allyl Isothiocyanate (AITC) was characterized by Infrared spectroscopy and refractive index.

The main infrared bands are congruent with the structure; the refractive index is 1.531.

Analyses references GLP Record Book 002/2013 pp. 2-3 Analysis N°2013000529	***CONFIDENTIAL REPORT*** *This information is the properly of RENOLAB. Information herein is confidential and must not be reproduced, revealed to unauthorized persons or sent outside without RENOLAB authorization.*

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

The study described in this report was conducted in compliance with the OECD Principles of Good Laboratory Practice and with the Italian Law Decree N. 50 of March 2nd, 2007, published on Gazzetta Ufficiale N. 86 of April 13th, 2007 - Enforcement of Directives 2004/9/EC and 2004/10/EC concerning the inspection and verification of Good Laboratory Practice (GLP) and aligning of laws, regulations and administrative provisions related to the application of the Principles of Good Laboratory Practice and to the control of their application on the tests performed on chemical substances.
There were no circumstances which may have affected the quality or integrity of the data.

REDOX snc acts as test site under commission of Renolab.

Principal investigator
(Andrea Borriero)

A Borriero 19/02/13
Date/Signature

QUALITY ASSURANCE STATEMENT

Study plan, experimental phase, draft report and final report of this study were audited by the Quality Assurance Unit. The experimental phase was audited as process audit. The dates are given below:

	Date of audit	Date of report
Study plan:	30/01/2013	30/01/2013
Experimental phase:	14-02 and 19/02/2013	19/02/2013
Final report:	19/02/2013	19/02/2013

Quality Assurance
(Patrizia Colombo)

19022013
Date / Signature

Infrared spectroscopy and refractive index characterization of sample Allyl Isothiocyanate (AITC) (batch QJHI20312)

Monza, 19th February 2013

Test Facility: REDOX s.n.c.
Viale Stucchi 62/26
I-20052 Monza (Italy)

Sponsor: RENOLAB
Via Altiero Spinelli, 12
44028 Poggio Renatico (FE)

The experiments reported herein were performed in Redox s.n.c. Analytical Labs in Monza (MI), Italy; all records are filed on the Redox GLP archive.
All the analyses have been carried out under GLP compliances - Ministero della Salute authorization n° 005/2011.

Experimental starting date: 14/02/2013

Experimental completion date: 19/02/2013

Submitted by: M. Calvi — Date: 19/02/2013

P. Annoni — Date: 19/02/2013

Approved by: A. Borriero (Principal investigator) — Date: 19/02/2013

1 – INTRODUCTION

The sample Allyl Isothiocyanate (AITC) (batch QJH120312) was characterized by Infrared spectroscopy and refractive index.

No reference was available.

2 – EXPERIMENTAL SECTION

2.1 Sample

Allyl Isothiocyanate (AITC) (batch QJHI20312) Analysis N°2013000529
Supplier: Renolab

2.2 FT-IR / ATR Spectroscopy (Fourier Transform Infra Red Spectroscopy with Attenuated Total Reflectance).

The FT-IR characterization was carried out by FT-IR/ATR Perkin Elmer Spectrum Two (SOP STR 078) equipment under the following conditions:

Range:	4000 – 450 cm^{-1}
Background:	Air
Resolution:	4 cm^{-1}

2.3 Refractive index

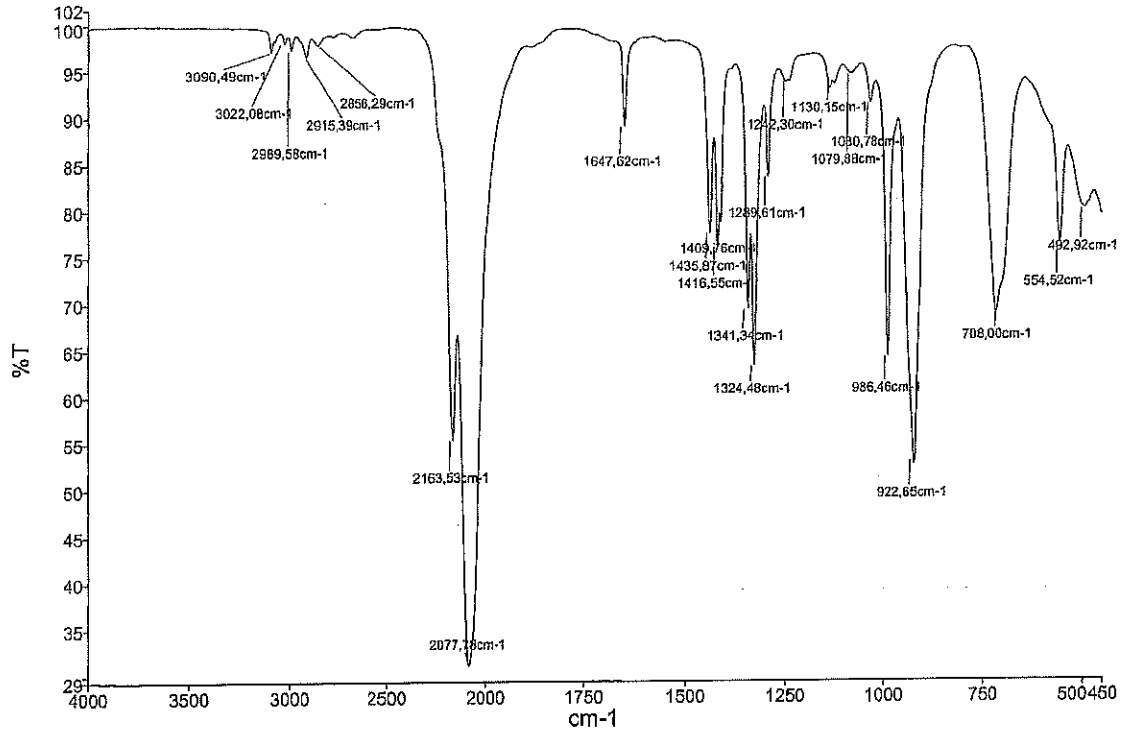
Refractive index (n^{D}_{20}) of sample was determined with refractometer Jena 183264 (SOP STR 064) at temperature of 20.2 °C and wavelength 589 nm.

3 – RESULTS

3.1 FT-IR / ATR Spectroscopy

In Fig.1 the FT-IR spectrum is reported.

Fig. 1 - FT-IR / ATR spectrum relative to Allyl Isothiocyanate (AITC) (batch QJHI20312).



The main characteristic bands are following reported:

3090 cm^{-1}: C-H stretching of CH_2 in vinyl group
3022 cm^{-1}: C-H stretching of CH in vinyl group
2990÷2856 cm^{-1}: C-H stretching of $-CH_2-$ central group
2078, and shoulder at 2164 cm^{-1}: -N=C=S out-of-phase stretching
1648 cm^{-1}: C=C stretching
1435÷1409 cm^{-1}: $=CH_2$ wagging (vinyl CH_2)
1341, 1324 cm^{-1}: $-CH_2-$ wagging (central CH_2)
987 cm^{-1}: CH wagging in R-$\underline{CH}$=CH_2
923 cm^{-1}: terminal CH_2 wagging in R-CH=$\underline{CH_2}$:
708 cm^{-1}: -N=C=S in-phase stretching

3.2 Refractive index

The value of refractive index results $n^{D}_{20} = 1.531$

4 – FINAL SUMMARY

Analysis N°: 2013000529

Test Facility: REDOX s.n.c. – Viale Stucchi 62/26 – 20052 MONZA (Italy)
Supplier: RENOLAB Via Altiero Spinelli, 12 44028 Poggio Renatico (FE)
Sample: Allyl Isothiocyanate (AITC) (batch QJHI20312)

Subject: Sample Allyl Isothiocyanate (AITC) (batch QJH120312) was analyzed for Infrared Spectroscopy characterization and determination of refractive index.

The main infrared bands are congruent with the structure; the refractive index is 1.531.

Analyst:

M. Calvi 14/2/13

P. Annoni 19/02/13

Principal investigator:

A. Borriero 19/02/13

Date of issue: February 19th, 2013

Quality Assurance:

P. Colombo 19022013

This study has been performed in compliance with the principles of Good Laboratory Practice.

6.9 APPENDIX I: IR spectroscopy and refractive index of AITC of natural origin

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REDOX snc – (Monza) Cert. BPL n°005/2011 Cert. GMP n°053/2012	Sponsor: **Renolab** PAGES IN FULL REPORT: 6	EXTERNAL REPORT NUMBER **051/13** **(Ed.1)**
DEPARTMENT NAME ***Analytical Chemistry & Process Safety Testing Labs***		DATE ISSUED: **19/02/13**

TITLE:

Infrared spectroscopy and refractive index characterization of sample natural Allyl Isothiocyanate (AITC) (batch 1050120806/11)

AUTHOR(S)	PRINCIPAL INVESTIGATOR
M. Calvi 19/2/13 **P. Annoni** 19/02/13	**A. Borriero** 19/02/13

SUMMARY

The sample natural Allyl Isothiocyanate (AITC) (batch 1050120806/11) was characterized by Infrared spectroscopy and refractive index.

The main infrared bands are congruent with the structure; the refractive index is 1.532.

Analyses references
GLP Record Book 003/2013 pp. 2-3
Analysis N°2013000530

Renolab 19/02/13

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

The study described in this report was conducted in compliance with the OECD Principles of Good Laboratory Practice and with the Italian Law Decree N. 50 of March 2nd, 2007, published on Gazzetta Ufficiale N. 86 of April 13th, 2007 - Enforcement of Directives 2004/9/EC and 2004/10/EC concerning the inspection and verification of Good Laboratory Practice (GLP) and aligning of laws, regulations and administrative provisions related to the application of the Principles of Good Laboratory Practice and to the control of their application on the tests performed on chemical substances.
There were no circumstances which may have affected the quality or integrity of the data.

REDOX snc acts as test site under commission of Renolab.

Principal investigator
(Andrea Borriero)

A Borriero 19/02/13
Date/Signature

QUALITY ASSURANCE STATEMENT

Study plan, experimental phase, draft report and final report of this study were audited by the Quality Assurance Unit. The experimental phase was audited as process audit. The dates are given below:

	Date of audit	Date of report
Study plan:	30/01/2013	19/02/2013
Experimental phase:	14/02-19/02/2013	19/02/2013
Final report:	19/02/2013	19/02/2013

Quality Assurance
(Patrizia Colombo)

19/02/13
Date / Signature

Infrared spectroscopy and refractive index characterization of sample natural Allyl Isothiocyanate (AITC) (batch 1050120806/11)

Monza, 19th February 2013

Test Facility: REDOX s.n.c.
Viale Stucchi 62/26
I-20052 Monza (Italy)

Sponsor: RENOLAB
Via Altiero Spinelli, 12
44028 Poggio Renatico (FE)

The experiments reported herein were performed in Redox s.n.c. Analytical Labs in Monza (MI), Italy; all records are filed on the Redox GLP archive.
All the analyses have been carried out under GLP compliances - Ministero della Salute authorization n° 49/2008.

Experimental starting date: 14/02/2013

Experimental completion date: 19/02/2013

Submitted by: M. Calvi — Date: 19/02/2013

P. Annoni — Date: 19/02/2013

Approved by: A. Borriero (Principal investigator) — Date: 19/02/2013

1 – INTRODUCTION

The sample natural Allyl Isothiocyanate (AITC) (batch) was characterized by Infrared spectroscopy and refractive index.
No reference was available.

2 – EXPERIMENTAL SECTION

2.1 Sample

Natural Allyl Isothiocyanate (AITC) (batch 1050120806/11) Analysis N°2013000530
Supplier: Renolab

19 02 2013

2.2 FT-IR / ATR Spectroscopy (Fourier Transform Infra Red Spectroscopy with Attenuated Total Reflectance).

The FT-IR characterization was carried out by FT-IR/ATR Perkin Elmer Spectrum Two (SOP STR 078) equipment under the following conditions:

Range:	4000 – 450 cm^{-1}
Background:	Air
Resolution:	4 cm^{-1}

2.3 Refractive index

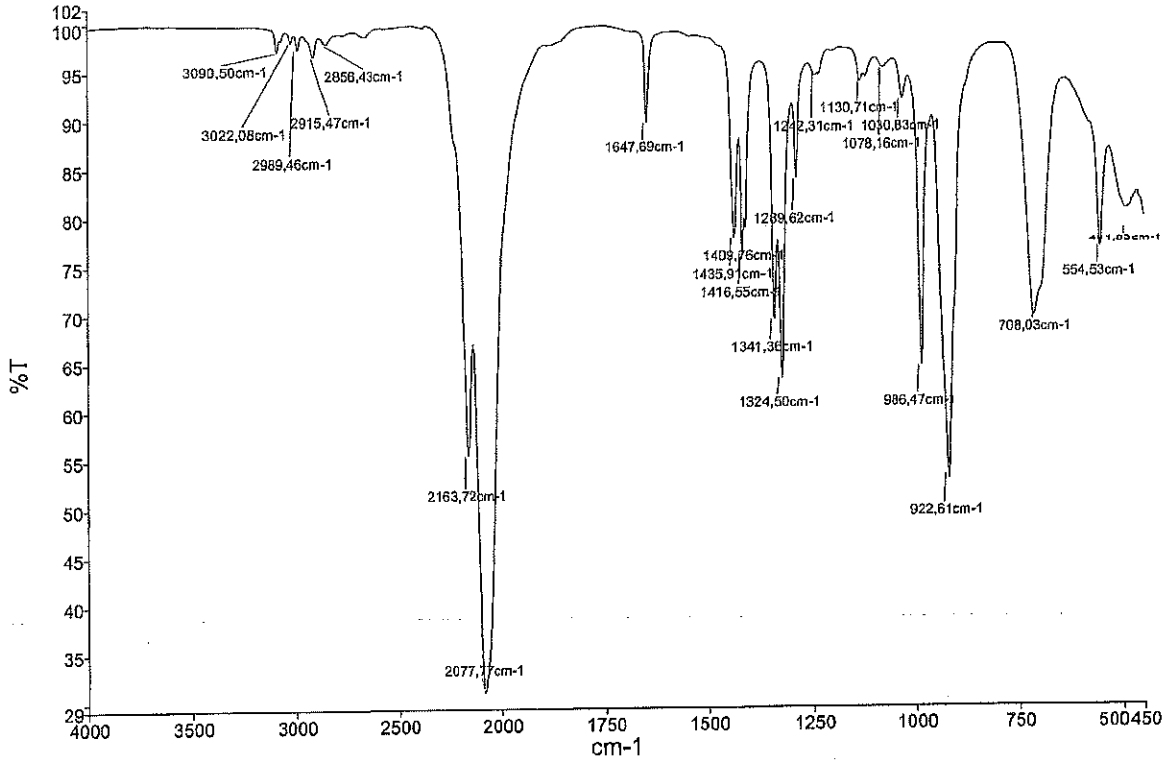
Refractive index (n^{D}_{20})of sample was determined with refractometer Jena 183264 (SOP STR 064) at temperature of 20.2 °C and wavelength 589 nm.

3 – RESULTS

3.1 FT-IR / ATR Spectroscopy

In Fig.1 the FT-IR spectrum is reported.

Fig. 1 - FT-IR / ATR spectrum relative to natural Allyl Isothiocyanate (AITC) (batch 1050120806/11).



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3091 cm^{-1}: C-H stretching of CH_2 in vinyl group
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2990÷2856 cm^{-1}: C-H stretching of –CH_2- central group
2078, and shoulder at 2164 cm^{-1}: -N=C=S out-of-phase stretching
1648 cm^{-1}: C=C stretching
1436÷1410 cm^{-1}: =CH_2 wagging (vinyl CH_2)
1341, 1325 cm^{-1}: -CH_2- wagging (central CH_2)
987 cm^{-1}: CH wagging in R-$\underline{CH}$=CH_2
923 cm^{-1}: terminal CH_2 wagging in R-CH=$\underline{CH_2}$:
708 cm^{-1}: -N=C=S in-phase stretching

3.2 Refractive index

The value of refractive index results n^{D}_{20} = 1.532

4 – FINAL SUMMARY

Analysis N°: 2013000530

Test Facility: REDOX s.n.c. – Viale Stucchi 62/26 – 20052 MONZA (Italy)
Supplier: RENOLAB Via Altiero Spinelli, 12 44028 Poggio Renatico (FE)
Sample: Natural Allyl Isothiocyanate (AITC) (batch 1050120806/11)

Subject: Sample Natural Allyl Isothiocyanate (AITC) (batch 1050120806/11) was analyzed for Infrared Spectroscopy characterization and determination of refractive index.

The main infrared bands are congruent with the structure; the refractive index is 1.532.

Analyst:

M. Calvi 19/2/13

R. Annoni 19/02/13

Principal investigator:

A. Borriero 19/02/13

Date of issue: February 19th, 2013

Quality Assurance:

P. Colombo 19/02/13

This study has been performed in compliance with the principles of Good Laboratory Practice.

NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 234

CARCINOGENESIS BIOASSAY OF ALLYL ISOTHIOCYANATE

(CAS NO. 57-06-7)

IN F344/N RATS AND B6C3F$_1$ MICE

(GAVAGE STUDY)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of chemically induced disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/ validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is comprised of four charter DHHS agencies: the National Cancer Institute, National Institutes of Health; the National Institute of Environmental Health Sciences, National Institutes of Health; the National Center for Toxicological Research, Food and Drug Administration; and the National Institute for Occupational Safety and Health, Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP TECHNICAL REPORT
ON THE

CARCINOGENESIS BIOASSAY OF ALLYL ISOTHIOCYANATE

(CAS NO. 57-06-7)

IN F344/N RATS AND B6C3F$_1$ MICE (GAVAGE STUDY)

NATIONAL TOXICOLOGY PROGRAM
Box 12233
Research Triangle Park
North Carolina 27709
and
Bethesda, Maryland 20205

October 1982

NTP-81-36
NIH Publication No. 83-1790

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NOTE TO THE READER

This is one in a series of experiments designed to determine whether selected chemicals produce cancer in animals. Chemicals selected for testing in the NTP carcinogenesis bioassay program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical is a potential hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

This study was initiated by the National Cancer Institute's Carcinogenesis Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program.

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room A-306, Landow Building, Bethesda, MD 20205 (301-496-1152) or at Research Triangle Park, NC 27709 (919-541-3991).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP.

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650).

Single copies of this carcinogenesis bioassay technical report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

TABLE OF CONTENTS

TABLES

FIGURES

APPENDIXES

CARCINOGENESIS BIOASSAY OF ALLYL ISOTHIOCYANATE

ALLYL ISOTHIOCYANATE

CAS NO. 57-06-7
C_4H_5NS Mol. Wt. 99.16

ABSTRACT

A 2-year carcinogenesis bioassay of food-grade allyl isothiocyanate (greater than 93% purity), a flavoring agent, was conducted by administering 12 or 25 mg/kg allyl isothiocyanate in corn oil five times per week by gavage to groups of 50 F344/N rats and 50 B6C3F1 mice of each sex for 103 weeks. Groups of 50 rats and 50 mice of each sex received corn oil alone and served as vehicle controls.

A single-dose study, a 14-day study, and a 13-week study were performed before the chronic study was conducted. Pathologic findings seen in the 14-day study at 50 mg/kg included a thickened mucosal surface of the stomach in rats and mice and a thickened urinary bladder wall in male mice. No gross or microscopic lesions were seen at the highest dose level (25 mg/kg) in the 13-week study.

In the chronic study, survival of dosed and control rats of each sex was comparable. Throughout the study, the mean body weights of high-dose male rats were lower than those of the controls, while during the last half of the study the mean body weights of the low-dose and high-dose female rats were higher than the mean body weights of the control animals. Final body weights in control and dosed groups were comparable.

Transitional-cell papillomas in the urinary bladder occurred in dosed male rats with a statistically significant trend ($P<0.05$; controls, 0/49, 0%; low-dose, 2/49, 4%; high-dose, 4/49, 8%). This tumor has not been observed among 568 untreated male control F344/N rats at this laboratory. The incidence of transitional-cell papillomas in male vehicle control rats in all laboratories in the NCI/NTP Bioassay Program is 1/994 (0.1%). Epithelial hyperplasia in the urinary bladder was also observed at increased incidences in dosed male rats (0/49, 1/49, 6/49). The hyperplasia did not occur in the same animals that had papillomas.

Fibrosarcomas in the subcutaneous tissue occurred in female rats with a statistically significant positive trend ($P<0.05$; controls, 0/50, 0%; low-dose, 0/50, 0%; high-dose, 3/50, 6%), but the incidence in the high-dose group was not significant when compared with that in the control group. The historical incidence of this lesion is 1/591 (0.2%) in untreated control female F344/N rats at this laboratory and 9/999 (0.9%) in female gavage control rats in all laboratories in the Bioassay Program.

Survival of control and dosed female mice, although comparable, was unusually low. Mean body weights of high-dose mice of each sex were higher than those of the controls throughout most of the study. Final body weights in control and dosed groups were comparable. The mice probably did not receive the maximum tolerated dose of allyl isothiocyanate.

The increased incidence of cytoplasmic vacuolization in the liver of dosed male mice was related to administration of allyl isothiocyanate (controls, 2/49, 4%; low-dose, 8/49, 16%; high-dose, 13/50, 26%).

Under the conditions of this bioassay, allyl isothiocyanate was carcinogenic for male F344/N rats, causing transitional-cell papillomas in the urinary bladder. Evidence for associating allyl isothiocyanate with subcutaneous fibrosarcomas in female F344/N rats was equivocal. Allyl isothiocyanate was not carcinogenic for B6C3F1 mice of either sex.

CONTRIBUTORS

The bioassay of allyl isothiocyanate was conducted at Southern Research Institute under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The chronic study was begun in March 1978 and completed in April 1980.

Principal Contributors at Southern Research Institute
Southern Research Institute
2000 Ninth Avenue South
Birmingham, Alabama 35255
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Pathologist

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Pathologist

Ms. L. Burford
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Ms. R. James
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Animal Care and Chemical Administration

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North Carolina 27709
and
Landow Building
Bethesda, Maryland 20205
(Evaluated the experiment, interpreted results, and reported findings)

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Dr. J. Fielding Douglas
Dr. Charles K. Grieshaber
Dr. Larry Hart
Dr. Joseph Haseman
Dr. James E. Huff
Dr. C. W. Jameson
Dr. Ernest E. McConnell
Dr. John A. Moore
Dr. Sherman F. Stinson
Dr. Raymond Tennant
Dr. Jerrold M. Ward

The pathology report and selected slides were evaluated on February 18, 1981 by the NTP Pathology Working Group, which included Drs. J. Ward, D. Goodman (Clement Associates), R. Kovatch (Tracor Jitco), S. Stinson, G. Reznik, G. Boorman, E. McConnell, and B. Gupta.

The chemicals used in this bioassay of allyl isothiocyanate were analyzed by the Midwest Research Institute, 425 Volker Blvd., Kansas City, Missouri 64110, and analysis of the corn oil mixtures and reanalysis of the bulk chemical were done by Southern Research Institute.

REVIEWERS

National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee

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SUMMARY OF PEER REVIEW COMMENTS ON THE BIOASSAY OF ALLYL ISOTHIOCYANATE

On June 23, 1981, this carcinogenesis bioassay report on allyl isothiocyanate underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts at an open meeting held in Building 101, National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. Williams, as a principal reviewer for the report on the bioassay of allyl isothiocyanate, agreed with the conclusions that, under the conditions of the bioassay, allyl isothiocyanate was carcinogenic to male F344/N rats, causing transitional-cell papillomas in the urinary bladder. Evidence for associating allyl isothiocyanate with subcutaneous fibrosarcomas in female rats was equivocal. The chemical was not carcinogenic for B6C3F1 mice of either sex. He stated that the discussion should emphasize that this compound was associated with only a low incidence of benign bladder tumors under conditions of exposure that are known to affect the physiology of urine excretion.

As the second principal reviewer, Dr. Hitchcock said there was quite low survival in control and high-dose female mice and suggested that some explanation should have been given for this. She noted the incidence of eye lesions which may have been due to groups of rats being housed near the light source without rotation of cages. Dr. Shore asked whether attention could be given to balancing cage position in the room. Dr. G. Boorman, NTP, replied that one problem with cage rotation is that it may enhance the chances for gavage errors; he further stated that the NTP was investigating this recurring phenomenon and would consider the option of cage rotation as well as reduced light intensity. Dr. Hitchcock asked that recent negative results with *Salmonella* be mentioned. Dr. Swenberg said that the discussion should include comment that allyl isothiocyanate may possibly be working as a tumor promoter.

Dr. Williams moved that the report on the bioassay of allyl isothiocyanate be accepted. Dr. Hitchcock accepted the motion, and the report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION

ALLYL ISOTHIOCYANATE

CAS NO. 57-06-7
C_4H_5NS Mol. Wt. 99.16

Allyl isothiocyanate is the major component in volatile oil of mustard, a flavoring agent prepared from seeds of black mustard (*Brassica nigra*) (Life Sciences Research Office, 1975). Synthetically prepared allyl isothiocyanate and volatile oil of mustard are approved by the U.S. Food and Drug Administration for use as flavoring agents (U.S. CFR, 1979); the Food Chemicals Codex (1972) specifies that the oil should contain not less than 93% allyl isothiocyanate. Allyl isothiocyanate is also found in cabbage, broccoli, kale, cauliflower, and horseradish (Mitchell and Jordan, 1974; Life Sciences Research Office, 1975; Hall, 1973).

Volatile oil of mustard is used in pickling spices and imitation pineapple flavoring (Kirk-Othmer, 1966). Allyl isothiocyanate may be present in the following foods: syrups (10-88 ppm), meats (87 ppm), condiments (52 ppm), baked goods (5.2 ppm), candy, ice cream, and ices (0.50 ppm), and nonalcoholic beverages (0.02-0.50 ppm) (Life Sciences Research Office, 1975). Allyl isothiocyanate is also used as a denaturant for alcohol and as a medicinal counter-irritant (Merck Index, 1976; Kirk-Othmer, 1965).

Approximately 33,000 pounds of allyl isothiocyanate were used by the food industry in the United States in 1970 (Life Sciences Research Office, 1975). The amount of synthetic allyl isothiocyanate produced in 1979 exceeded 1,000 pounds, but specific production figures are not available (USITC, 1979). Thirty-two thousand metric tons of mustard seed were imported into the United States in 1978 (Kirk-Othmer, 1980).

The oral LD_{50} value of allyl isothiocyanate is reported to be 339 mg/kg for Osborne-Mendel rats (Jenner et al., 1964) and 490 mg/kg for male rats of an unspecified strain (Vernot et al., 1977). The subcutaneous LD_{50} value for white mice is 80 mg/kg (Klesse and Lukoschek, 1955).

Administration of allyl isothiocyanate has been shown to affect various functions and organs in the rat. Radioiodine uptake by the thyroid was depressed and the relative weight of the thyroid was increased in male Wistar rats administered 2-to 5-mg doses of allyl isothiocyanate by gavage daily for 1 to 60 days (Langer and Greer, 1968; Langer and Stole, 1965). Hyperplastic areas were observed in the thyroid of female Holtzman rats 12 days after they received two 100 mg/kg subcutaneous doses of allyl isothiocyanate (Nishie and Daxenbichler, 1980). The blood coagulation time for male Sprague-Dawley rats given daily 0.5 mg intraperitoneal injections of allyl isothiocyanate for 30 days was 60% of the value for controls (Muztar et al., 1979b). A twofold increase in urine volume, an increase in the total amount of uric acid, creatinine, and glucose excreted during a 24-hour period, and an increase in the concentration of uric acid in the urine compared with that of controls were observed in male Sprague-Dawley rats fed diets containing 100 or 300 ppm allyl isothiocyanate (Muztar et al., 1979a; Muztar et al., 1979b).

Epithelial hyperplasia of the nonglandular portion of the stomach, with acute to subacute ulcers 2 to 6.5 mm in diameter, was observed in all Osborne-Mendel rats of either sex administered 50 mg/kg allyl isothiocyanate by gavage for 20 days and in 50% of the rats receiving 20 mg/kg. Minor inflammatory foci were observed in the liver of rats receiving the higher dose (Hagan et al., 1967).

Allyl isothiocyanate was not mutagenic in *Bacillus subtilis* H17 and M45, *Escherichia coli* WP2, or *Salmonella typhimurium* TA 98, 100, 1535, or 1537 (with or without metabolic activation) (Oda et al., 1978; Eder et al., 1980; NTP, 1981). Allyl isothiocyanate was fetotoxic for Holtzman rats (Nishie and Daxenbichler, 1980),

but was not found to be teratogenic in Wistar rats (Ruddick et al., 1976).

The Food and Drug Administration has prepared three reviews on oil of mustard (90% allyl isothiocyanate), a food additive generally recognized as safe (NTIS, 1972; NTIS, 1973; NTIS, 1975). These reviews emphasize the lack of data on the carcinogenicity and toxicity of these substances. The FDA cites some evidence for increased fetal deaths and resorptions in rodents when oil of mustard is administered at 28.0 mg/kg for 10 consecutive days (from days 6 to 15 of gestation) to pregnant mice (albino CD-1 outbred mice). Other teratology studies in rats, hamsters, and rabbits were considered negative (NTIS, 1973). A select committee of the Federation of American Societies for Experimental Biology (FASEB) stated that "more definitive toxicological studies" on oil of mustard were warranted. Using the data available in 1975, FASEB concluded that there was no indication that allyl isothiocyanate was a hazard to the public at levels currently used in food (NTIS, 1973).

The NCI/NTP Bioassay Program tested allyl isothiocyanate because it is a widely used food additive that had not been tested for carcinogenicity.

II. MATERIALS AND METHODS

CHEMICAL ANALYSIS

DOSAGE PREPARATION

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Study Design

Clinical Examinations and Pathology

Data Recording and Statistical Methods

CHEMICAL ANALYSIS

Food-grade allyl isothiocyanate (CAS No. 57-06-7), greater than 93% allyl isothiocyanate, was obtained from Arsynco, Inc. (Carestadt, NJ) in a single batch (Lot No. 532251).

The results of the analyses performed at Midwest Research Institute (Appendix E) indicated the following: elemental analyses agreed with theoretical values; gas-liquid chromatography on two different systems detected at least six minor impurities with areas totaling less than 1% of the major peak; thin-layer chromatography in two systems detected only one spot; the infrared and ultraviolet spectra were consistent with the structure and spectra reported in the literature (Sadtler Research Laboratories); and the nuclear magnetic resonance spectrum was consistent with the structure. The nuclear magnetic resonance spectrum indicated the presence of a minor impurity that could be the thiocyanate. The identity of this minor impurity was not pursued.

Southern Research Institute analyzed the chemical periodically throughout the study by gas-liquid chromatography and infrared spectroscopy. The results indicated no breakdown of the bulk material during the study.

DOSAGE PREPARATION

Dosage mixtures of allyl isothiocyanate were prepared daily in the single-dose and 14-day studies and were prepared weekly in the 13-week and chronic studies. Mixtures were obtained by pipetting the appropriate amount of the chemical in a beaker and dissolving it in a small amount of corn oil. This stock solution was diluted with additional corn oil to the desired final volume. Concentrations of the test substance were based on the volume of the chemical in relation to the volume of corn oil.

Analysis of the stability of allyl isothiocyanate in corn oil was performed at Midwest Research Institute by assaying samples of corn oil mixtures containing 0.05% test chemical that had been stored at room temperature for 7 days (Appendix F). The corn oil/allyl isothiocyanate solutions were then diluted with anhydrous ethyl ether, and the concentration of the test chemical was determined by vapor-phase chromatography. Allyl isothiocyanate was found to be stable in corn oil for 7 days at room temperature with a recovery of 99.5%. Selected batches of corn oil gavage mixtures administered during the chronic study were analyzed at Southern Research Institute to determine the adequacy of preparation; differences between the mean sample concentration and the targeted concentration were 0.01% (v/v) or less (Table G1).

Four samples of corn oil gavage mixtures prepared and analyzed at Southern Research Institute were shipped to either Midwest Research Institute or Raltech Scientific Services, Inc., for referee analysis of allyl isothiocyanate. The results from the three laboratories were in agreement.

PRECHRONIC STUDIES

Single-Dose Study

Groups of five F344/N rats of each sex were administered a single dose of allyl isothiocyanate (25, 50, 100, 200, or 400 mg/kg body weight) in corn oil by gavage. Groups of five B6C3F1 mice of each sex received 50, 100, 200, 400, or 800 mg/kg allyl isothiocyanate by the same route. No controls were used.

Animals were observed twice daily for 16 days. Weights were taken on the day of dosing and then on day 15. The peritoneal cavities were examined in male mice administered 200, 400, or 800 mg/kg and in female mice administered 100, 200, or 400 mg/kg.

Further details of the study are presented in Table 1.

Fourteen-Day Study

Groups of five F344/N rats of either sex were administered 25, 50, 100, 200, or 400 mg/kg allyl isothiocyanate in corn oil by gavage for 14 consecutive days (Table 1). Groups of B6C3F1 mice received 3, 6, 12, 25, or 50 mg/kg by the same route. No controls were used.

Rats and mice were observed twice daily and were weighed on days 1 and 15 of the study. Gross necropsies were performed on all animals.

Thirteen-Week Study

Thirteen-week studies were conducted to evaluate the cumulative toxicity of allyl isothiocyanate and to determine the doses to be used in the chronic studies.

Groups of 10 rats and mice of each sex received 1.5, 3, 6, 12, or 25 mg/kg allyl isothiocyanate by gavage 5 days per week for 13 weeks (Table 1). Vehicle controls received corn oil alone.

All animals were checked for mortality and clinical signs of toxicity and morbidity twice daily. Moribund animals were killed and necropsied. Individual animals were weighed weekly.

From days 92 to 96, survivors were killed with carbon dioxide. Necropsies were performed on animals that survived to day 92 and on all animals found dead, unless precluded in whole or part by autolysis or cannibalism. The following specimens were examined histologically in vehicle-control and high-dose groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, bone marrow, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, cecum, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, thymus, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, and pituitary. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

CHRONIC STUDY

Study Design

Groups of 50 rats and 50 mice of each sex received 12 or 25 mg/kg allyl isothiocyanate in corn oil by gavage 5 times per week (Monday through Friday) for 103 weeks (Table 1). Groups of 50 rats and 50 mice of each sex received corn oil on the same schedule and served as vehicle controls.

Control and dosed groups were of the same strain, sex, and age range and were from the same source and shipment. All animals were housed in the same room, and no other chemicals were on test in that room. Neither cages nor racks were rotated. The animal cages were housed on two racks, each rack having six levels. On one rack, high-dose males were on the top two levels, high-dose females were on the middle two levels, and low-dose males were on the bottom two levels. On the other rack, low-dose females were placed on the top two levels, control males were on the middle two levels, and control females were on the bottom two levels. All aspects of animal care and maintenance were similar. Animals were randomized to control and dosed groups as described in Table 1. Chronic studies for rats and mice began in March 1978.

Clinical Examinations and Pathology

All animals were observed twice daily for signs of morbidity and mortality. Clinical signs and body weights by cage were recorded every 4 weeks. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. Moribund animals and animals that survived to the end of the bioassay were killed with carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, bone marrow, femur, thymus, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/ uterus, brain, and pituitary. Oil Red O on frozen sections was used to more clearly

define the nature of cytoplasmic vacuolization in the livers of male mice.

Necropsies were performed on all animals found dead and on those killed at the end of the study, unless precluded in whole or in part by autolysis or cannibalism. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

The pathology report and selected slides were evaluated by the NTP Pathology Working Group as described by Ward et al. (1978). The diagnoses represent a consensus of contracting pathologists and the NTP Pathology Working Group.

Data Recording and Statistical Methods

Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time that they died of other than natural causes or were found to be missing; animals dying from natural causes were not statistically censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) extensions of Cox's methods for testing for a dose-related trend.

The incidence of neoplastic or nonneoplastic lesions has been given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators included only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

For the statistical analysis of tumor incidence data, two different methods of adjusting for intercurrent mortality were employed. Each used the classical methods for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high-and low-dose groups with controls and tests for overall dose-response trends.

The first method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "fatal"; i.e., they either directly or indirectly caused the death of the animal. According to this approach, the proportions of tumor-bearing animals in the dosed and control groups were compared at each point in time at which an animal died with a tumor of interest. The denominators of these proportions were the total number of animals at risk in each group. These results, including the data from animals killed at the end of the study, were then combined by the Mantel-Haenszel methods to obtain an overall P-value. This method of adjusting for intercurrent mortality is the life table method of Cox (1972) and of Tarone (1975).

The second method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "incidental"; i.e., they were merely observed at autopsy in animals dying of an unrelated cause. According to this approach, the proportions of animals found to have tumors in dosed and control groups were compared in each of five time intervals: 0-52 weeks, 53-78 weeks, 79-92 weeks, week 93 to the week before terminal kill, and the terminal kill period. The denominators of these proportions were the number of animals actually autopsied during the time interval. The individual time interval comparisons were then combined by the previously described methods to obtain a single overall result. (See Peto et al., 1980, for the computational details of both methods.)

In addition to these tests, one other set of statistical analyses was carried out and reported in the tables analyzing primary tumors; the Fisher's exact test for pairwise comparisons and the Cochran-Armitage linear trend test for dose-response trends (Armitage, 1971; Gart et al., 1979). The tests were based on the overall proportion of tumor-bearing animals. All reported P values are one-sided. For studies in which there is little effect of compound administration on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death.

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Experimental Design				
Size of Test Groups	5 males, 5 females of each species	5 males, 5 females of each species	10 males, 10 females of each species	50 males, 50 females of each species
Doses	Rats: 25, 50, 100, 200, or 400 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight Mice: 50, 100, 200, 400, or 800 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight.	Rats: 25, 50, 100, 200, or 400 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight Mice: 3, 6, 12, 25, or 50 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight	Rats and mice: 1.5, 3, 6, 12, or 25 mg/kg body weight allyl isothiocyanate in corn oil; vehicle control, corn oil only, volume: rats, 5 ml/kg body weight; mice, 10 ml/kg body weight	Rats and mice: low dose 12 mg/kg body weight allyl isothiocyanate in corn oil; high dose 25 mg/kg body weight allyl isothiocyanate in corn oil; vehicle control: corn oil; volume: rats, 5 ml/kg body weight; mice, 10 ml/kg body weight
Duration of Dosing	Rats and mice: single dose; killed on day 16	Rats: 14 consecutive days; killed on days 16-17 Mice: 14 consecutive days; killed on days 17-31	Rats and mice: 13 weeks, 5 days per week; killed on days 92-96	Rats and mice: 103 weeks; 5 days per week; killed at week 104-106
Type and Frequency of Observation	Observed twice daily for mortality	Observed twice daily for mortality	Observed twice daily for morbidity and mortality	Observed twice daily for morbidity and mortality
Necropsy and Histologic Examination	Peritoneal cavity examined in male mice receiving 200, 400, or 800 mg/kg and in female mice receiving 100, 200, or 400 mg/kg	All animals necropsied	Gross necropsy performed on all animals; histologic examination performed on all vehicle controls and all animals receiving 25 mg/kg	Gross necropsy and histologic examination performed on all animals

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS (Continued)

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Animals and Animal Maintenance				
Species	F344/N Rats; B6C3F1 Mice	F344/N Rats; B6C3F1 Mice	F344/N Rats; B6C3F1 Mice	F344/N Rats; B6C3F1 Mice
Animal Source	Frederick Cancer Research Center (Frederick, MD)	Same as single-dose study	Same as single-dose study	Harlan Industries, Inc. (Indianapolis, IN)
Time Held Before Start of Test	Rats: 9 days Mice: 8 days	Rats: 8 days Mice: 8 days	Rats: 5 days Mice: 5 days	Rats: 16 days Mice: 16 days
Age When Placed on Study	35 days old	35 days old	35 days old	Rats: 39 days old Mice: 57 days old
Age When Killed	51 days old	Rats: 51-52 days old Mice: 52-66 days old	127-131 days old	Rats: 767 days old Mice: 785 days old
Method of Animal Distribution	Randomized to cages using table of random numbers; cages randomized to test groups using another table of random numbers	Same as single-dose study	Same as single-dose study	Same as single-dose study
Feed	Wayne Lab Blox® Allied Mills, Inc. (Chicago, IL) Available *ad libitum*	Same as single-dose study	Same as single-dose study	Same as single-dose study
Bedding	Beta Chips®, hardwood chips, Northeastern Products Corp. (Warrensburg, NY)	Same as single-dose study	Same as single-dose study	Same as single-dose study
Water	Tap water in glass bottles available *ad libitum*	Same as single-dose study	Tap water via automatic system, Edstrom Industries, Inc. (Waterford, WI)	Same as 13-week study
Cages	Stainless steel, Hahn Roofing and Sheet Metal Co. (Birmingham, AL)	Same as single-dose study	Polycarbonate Lab Products, Inc. (Garfield, NJ)	Same as 13-week study

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS (Continued)

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Animals and Animal Maintenance				
Animals Per Cage	5	5	5	5
Cage Filters	Fiberglass	Fiberglass	Disposable spun-bonded Polyester Dupont #2024 Snow Filtration Co. (Cincinnati, OH)	Same as 13-week study
Animal Room Environment	23° ± 3°C; humidity uncontrolled; 15 air changes per hr. 9 hrs fluorescent light	Same as single-dose study	23°±3°C; humidity uncontrolled; 15 air changes per hr. 12 hrs fluorescent light	23°±3°C; humidity uncontrolled; 15 air changes per hr. 12 hrs fluorescent light
Other Chemicals on Test in Same Room	Rats and mice: ethyl acrylate, eugenol, D-mannitol;	Rats: ethyl acrylate, eugenol, D-mannitol; Mice: ethyl acrylate, eugenol, D-mannitol; stannous chloride, ziram, propyl gallate, zearalenone	None	None
Chemical/Vehicle Mixture				
Preparation	Allyl isothiocyanate mixed with Mazola® corn oil to concentration of highest dose (stock mixture); stock mixture diluted with corn oil to make other doses	Same as single-dose study	Same as single-dose study	Same as single-dose study
Frequency of Preparation	Mixture prepared daily	Mixture prepared daily	Mixture prepared once each week	Mixture prepared once each week
Storage Conditions		Excess mixture discarded		Dosing mixture stored at 5°C for no longer than 10 days

III. RESULTS

RATS

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

PRECHRONIC STUDIES

Single-Dose Study

All animals survived to the end of the 16-day observation period. The following average weight increases over the initial weight (on day 0) were measured:

Dose (mg/kg)	Weight Increase (Percent)	
	Males	Females
25	69	40
50	58	45
100	61	44
200	50	38
400	31	20

Other signs of toxicity seen in male rats receiving 200-400 mg/kg included inactivity, watery eyes, and ruffled fur. All signs were gone by day 9 in the 400 mg/kg group and by day 3 in the 200 mg/kg group. Female rats also exhibited inactivity and ruffled fur. Since no rats died during the course of those studies, the highest dose for the 14-day study was set at 400 mg/kg.

Fourteen-Day Study

All rats administered 200 or 400 mg/kg allyl isothiocyanate died before the end of the study (Table 2). Animals administered 100 mg/kg gained less weight than did animals receiving lower doses. A thickened mucosal surface of the stomach was seen in groups of males and females administered 50-400 mg/kg, and adhesion of the stomach to the peritoneum was observed in groups of male rats receiving 50-400 mg/kg and in groups of female rats receiving 100-400 mg/kg (Table 3).

Toxic signs were seen at all dose levels. These signs included inactivity and ruffled fur and were most severe at the 400 mg/kg dose level. Due to the toxicity and pathologic effects observed, the highest dose for the 13-week study was set at 25 mg/kg.

TABLE 2. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF RATS RECEIVING ALLYL ISOTHIOCYANATE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weight (grams)		
		Initial	Final	Change *(b)*
Males				
25	5/5	96.6 ± 5.0	147.0 ± 6.6	+50.4 ± 2.8
50	5/5	85.8 ± 3.9	127.2 ± 4.1	+41.4 ± 2.3
100	5/5	92.8 ± 7.1	113.0 ± 6.1	+20.2 ± 2.2
200	0/5*(c)*	*(d)*	*(d)*	*(d)*
400	0/5*(e)*	*(d)*	*(d)*	*(d)*
Females				
25	5/5	82.6 ± 2.7	113.2 ± 1.7	+30.6 ± 2.3
50	5/5	77.4 ± 3.5	105.6 ± 3.2	+28.2 ± 2.6
100	5/5	84.8 ± 3.0	105.8 ± 3.8	+21.0 ± 2.7
200	0/5*(f)*	*(d)*	*(d)*	*(d)*
400	0/5*(g)*	*(d)*	*(d)*	*(d)*

(a) Number surviving/number initially in the group. All calculations refer only to the survivors of each group.
(b) Mean weight change of the survivors of the group ± standard error of the mean.
(c) Days of death: 2, 2, 3, 8, 9
(d) No data are presented due to the 100% mortality in this group.
(e) Days of death: 2, 2, 2, 2, 4
(f) Days of death: 2, 2, 6, 8, 9
(g) Days of death: 2, 2, 2, 2, 3

TABLE 3. INCIDENCE OF COMPOUND-RELATED EFFECTS OBSERVED IN RATS AT NECROPSY IN THE 14-DAY STUDY OF ALLYL ISOTHIOCYANATE

Dose (mg/kg)	Thickened Mucosal Surface of Stomach	Adhesion of Stomach to Peritoneum
Males		
25	0/5	0/5
50	5/5	1/5
100	5/5	4/5
200	4/5*(a)*	5/5*(a)*
400	1/5*(a)*	3/5*(a)*
Females		
25	0/5	0/5
50	5/5	0/5
100	5/5	2/5
200	3/5*(a)*	4/5*(a)*
400	3/5*(a)*	4/5*(a)*

(a) See Table 2 for days of death.

Thirteen-Week Study

No compound-related deaths or histopathologic effects in the stomach or other tissues were observed. Mean body weight gains of control and dosed groups were comparable (Table 4). In this study, the highest dose level (25 mg/kg) had no effect on either male or female F344/N rats.

Doses of 12 and 25 mg/kg allyl isothiocyanate, administered five times per week by gavage, were selected for rats in the chronic study because compound-related gross pathologic effects were observed in the 14-day study at 50 mg/kg.

TABLE 4. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE FOR 13 WEEKS

Dose (mg/kg)*(a)*	Survival *(b)*	Mean Body Weight (grams)			Weight Change Relative to Controls *(d)* (Percent)
		Initial	Final	Change *(c)*	
Males					
0*(e)*	10/10	65.4 ± 3.4	309.8 ± 5.4	+244.4 ± 3.8	
1.5	10/10	65.9 ± 2.8	322.5 ± 6.2	+256.6 ± 4.8	+5.0
3	10/10	67.2 ± 2.6	321.0 ± 5.2	+253.8 ± 4.2	+3.8
6	10/10	67.2 ± 3.9	318.4 ± 5.4	+251.2 ± 4.9	+2.8
12	10/10	66.9 ± 2.9	314.5 ± 5.4	+247.6 ± 4.8	+1.3
25	10/10	66.7 ± 4.4	303.4 ± 8.8	+236.7 ± 7.5	−3.2
Females					
0*(e)*	10/10	56.1 ± 1.8	191.9 ± 3.1	+135.8 ± 4.1	
1.5	10/10	60.0 ± 2.1	194.7 ± 4.4	+134.7 ± 5.1	−0.8
3	10/10	64.0 ± 2.3	196.4 ± 4.0	+132.4 ± 4.1	−2.5
6	10/10	60.8 ± 2.4	195.3 ± 3.6	+134.5 ± 2.1	−1.0
12	10/10	59.8 ± 1.9	191.4 ± 3.0	+131.6 ± 3.8	−3.1
25	10/10	62.6 ± 2.7	192.9 ± 4.4	+130.3 ± 3.3	−4.1

(a) Allyl isothiocyanate in corn oil was administered 5 days per week.
(b) Number surviving/number initially in the group.
(c) Mean weight change of the group ± standard error of the mean.
(d) Weight change of the dosed group relative to that of the controls ◘

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

(e) Vehicle controls received corn oil alone.

CHRONIC STUDY

Body Weights and Clinical Signs

Throughout the study, the mean body weights of high-dose male rats were lower than those of the controls, and during the last half of the study the mean body weights of both low- and high-dose female rats were higher than those of the controls (Figure 1, and Appendix H, Table H1). No compound-related clinical signs were observed.

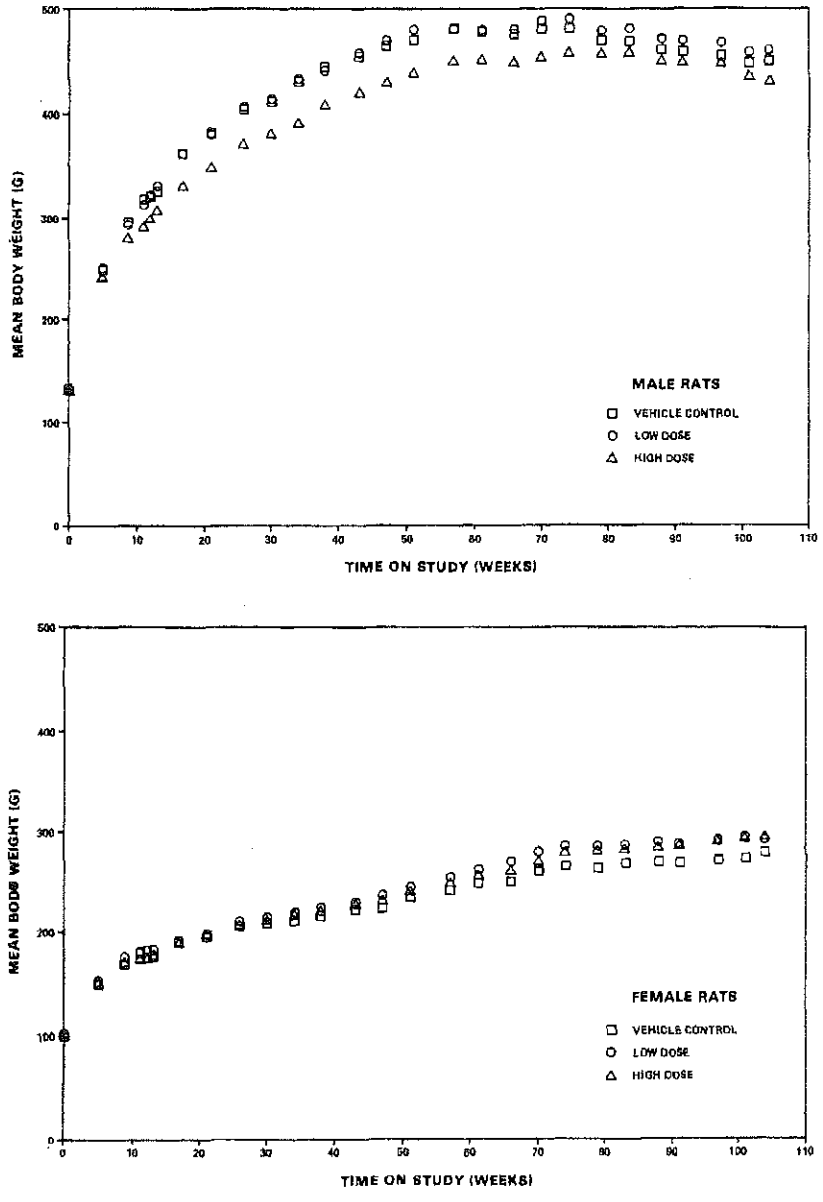

Figure 1. Growth Curves for Rats Administered Allyl Isothiocyanate by Gavage.

Survival

Estimates of the probabilities of survival of male and female rats administered allyl isothiocyanate by gavage at the doses of this bioassay, together with those of the control groups, are shown by the Kaplan and Meier curves in Figure 2. Two male rats were accidentally killed, one in the low-dose group at week 54 and one in the high-dose group at week 68. Two female rats in the low-dose group were accidentally killed at week 54. These deaths were due to gavage error. No significant differences in survival were observed. One control male, one low-dose male, and two low-dose females died during weeks 104-106. In the statistical analyses reported in Tables 6 and 7, no distinction was made between these animals and those killed during the termination period.

In male rats, 37/50 (74%) of the controls, 32/50 (64%) of the low-dose, and 33/50 (66%) of the high-dose group lived to the termination period of the study at 104-106 weeks. In female rats, 35/50 (70%) of the controls, 29/50 (58%) of the low-dose, and 33/50 (66%) of the high-dose group lived to the end of the study at 104-106 weeks.

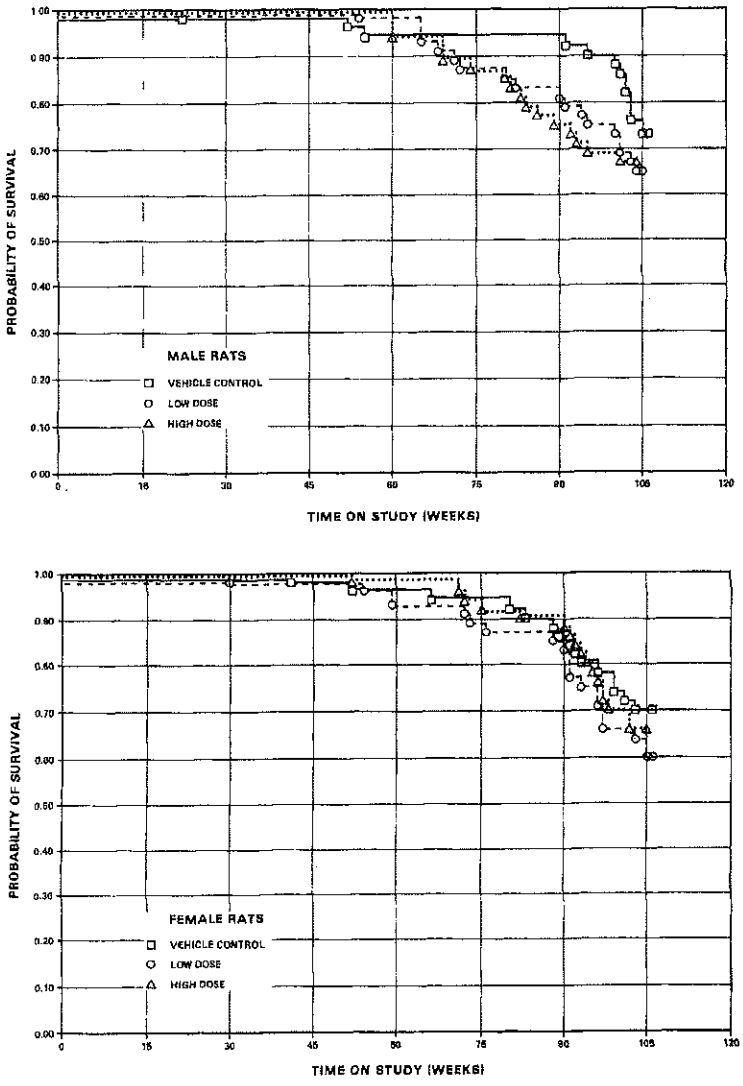

Figure 2. Survival Curves for Rats Administered Allyl Isothiocyanate by Gavage.

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; Tables A3 and A4 give the survival and tumor status for each individual animal in the male rat and female rat studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2. Tables 6 and 7 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Subcutaneous Tissue: Fibrosarcomas were observed in 3/50 (6%) high-dose female rats; none were seen in the control and low-dose groups. The results of all three trend tests were significant ($P<0.05$), but comparisons between the high-dose and control groups were not significant.

Hematopoietic System: Leukemia was observed in dosed male rats with a statistically significant positive trend ($P<0.05$; incidence: control, 2/50, 4%; low-dose 6/50, 12%; high-dose, 8/50, 16%). The incidence in the male high-dose group was significantly higher ($P<0.05$) than that in the control group. This leukemia, designated here as undifferentiated leukemia, is the typical leukemia of F344/N rats and is variously described as mononuclear cell leukemia. Fischer rat leukemia, or monocytic leukemia.

Urinary Bladder: Transitional-cell papillomas occurred in dosed male rats with a statistically significant ($P<0.05$) positive trend. Incidences in the control, low-dose, and high-dose groups were 0/49 (0%), 2/49 (4%), and 4/49 (8%). One female rat in the high-dose group had this lesion; the results in female rats were not significant. Epithelial hyperplasia was seen in 1/49 (2%) low-dose and 6/49 (12%) high-dose male rats. Both the overall trend and the increase at the high dose were statistically significant ($P<0.05$). Incidences of bladder lesions are given in Table 5.

Three of the tumors were large polypoid masses. The other lesions were small. Two of the large papillomas had a prominent myxomatous stroma. The hyperplasias were focal and small; a few were associated with mild inflammation. Urinary calculi were not observed in any animals in this study.

Eye: An increased incidence of nonneoplastic lesions consisting of retinopathy and cataract formation was observed in high-dose male rats and in low-dose female rats. Retinopathy was seen in 9/50 (18%) control males, 6/50 (12%) low-dose males, 39/50 (78%) high-dose males, 4/50 (8%) control females, 35/50 (70%) low-dose females, and 11/50 (22%) high-dose females. Cataract formation was observed in 7/50 (14%) control males, 6/50 (12%) low-dose males, 13/50 (26%) high-dose males, 2/50 (4%) control females, 33/50 (66%) low-dose females, and 9/50 (18%) high-dose females. The incidence of retinopathy and cataract formation correlated with the placement of the cages. The animals that occupied the two top levels of the racks (i.e., high-dose males and low-dose females) had the highest incidence of eye effects.

TABLE 5. INCIDENCE OF RATS WITH BLADDER LESIONS IN THE CHRONIC STUDY WITH ALLYL ISOTHIOCYANATE

	Incidence					
	Males			Females		
	Vehicle Control	Low Dose	High Dose	Vehicle Control	Low Dose	High Dose
Animals examined	49	49	49	49	49	50
Lesion:						
Transitional-Cell Papilloma	0	2	4	0	0	1
Epithelial Hyperplasia	0	1	6 *(a)*	0	0	1
Nodular Hyperplasia	0	0	1	0	0	0

(a) None of these animals had papillomas.

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Skin: Squamous Cell Papilloma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	0/50 (0%)	4/50 (8%)
Adjusted *(c)*	7.6%	0.0%	12.1%
Terminal *(d)*	2/38 (5%)	0/33 (0%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.331	P=0.152N	P=0.418
Incidental Tumor Test	P=0.292	P=0.159N	P=0.364
Cochran-Armitage Trend, Fisher Exact Tests	P=0.393	P=0.121N	P=0.500
Skin: Squamous Cell Papilloma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	0/50 (0%)	6/50 (12%)
Adjusted *(c)*	10.1%	0.0%	17.2%
Terminal *(d)*	3/38 (8%)	0/33 (0%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.203N	P=0.086N	P=0.284
Incidental Tumor Test	P=0.234N	P=0.090N	P=0.331
Cochran-Armitage Trend, Fisher Exact Tests	P=0.260	P=0.059N	P=0.370
Subcutaneous Tissue: Fibrosarcoma			
Tumor Rates			
Overall *(b)*	5/50 (10%)	5/50 (10%)	1/50 (2%)
Adjusted *(c)*	12.5%	14.1%	2.8%
Terminal *(d)*	4/38 (11%)	4/33 (12%)	0/33 (0%)
Statistical Tests *(e)*			
Life Table	P=0.133N	P=0.542	P=0.154N
Incidental Tumor Test	P=0.123N	P=0.628N	P=0.215N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.088N	P=0.630	P=0.102N
Subcutaneous Tissue: All Sarcomas			
Tumor Rates			
Overall *(b)*	6/50 (12%)	8/50 (16%)	2/50 (4%)
Adjusted *(c)*	14.5%	20.5%	5.1%
Terminal *(d)*	4/38 (11%)	5/33 (15%)	0/33 (0%)
Statistical Tests *(e)*			
Life Table	P=0.189N	P=0.304	P=0.209N
Incidental Tumor Test	P=0.088N	P=0.540	P=0.198N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.124N	P=0.387	P=0.134N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	3/49 (6%)	2/49 (4%)	3/48 (6%)
Adjusted *(c)*	7.2%	6.3%	8.8%
Terminal *(d)*	1/37 (3%)	2/32 (6%)	2/31 (6%)
Statistical Tests *(e)*			
Life Table	P=0.512	P=0.556N	P=0.590
Incidental Tumor Test	P=0.545N	P=0.426N	P=0.541N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.577	P=0.500N	P=0.651

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	2/50 (4%)	6/50 (12%)	8/50 (16%)
Adjusted *(c)*	4.7%	17.1%	21.6%
Terminal *(d)*	0/38 (0%)	4/33 (12%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.024	P=0.093	P=0.030
Incidental Tumor Test	P=0.006	P=0.070	P=0.009
Cochran-Armitage Trend, Fisher Exact Tests	P=0.039	P=0.134	P=0.046
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	2/50 (4%)	7/50 (14%)	8/50 (16%)
Adjusted *(c)*	4.7%	19.1%	21.6%
Terminal *(d)*	0/38 (0%)	4/33 (12%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.027	P=0.054	P=0.030
Incidental Tumor Test	P=0.011	P=0.060	P=0.009
Cochran-Armitage Trend, Fisher Exact Tests	P=0.044	P=0.080	P=0.046
Liver: Neoplastic Nodule			
Tumor Rates			
Overall *(b)*	2/50 (4%)	0/50 (0%)	5/50 (10%)
Adjusted *(c)*	5.3%	0.0%	15.2%
Terminal *(d)*	2/38 (5%)	0/33 (0%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.085	P=0.270N	P=0.162
Incidental Tumor Test	P=0.085	P=0.270N	P=0.162
Cochran-Armitage Trend, Fisher Exact Tests	P=0.112	P=0.247N	P=0.218
Urinary Bladder: Transitional-Cell Papilloma			
Tumor Rates			
Overall *(b)*	0/49 (0%)	2/49 (4%)	4/49 (8%)
Adjusted *(c)*	0.0%	5.5%	12.1%
Terminal *(d)*	0/37 (0%)	1/32 (3%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.030	P=0.209	P=0.049
Incidental Tumor Test	P=0.048	P=0.356	P=0.049
Cochran-Armitage Trend, Fisher Exact Tests	P=0.038	P=0.247	P=0.059
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	7/47 (15%)	12/49 (24%)	4/49 (8%)
Adjusted *(c)*	18.0%	30.6%	11.7%
Terminal *(d)*	5/36 (14%)	6/32 (19%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.326N	P=0.107	P=0.336N
Incidental Tumor Test	P=0.270N	P=0.236	P=0.462N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.204N	P=0.178	P=0.238N

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	7/47 (15%)	13/49 (27%)	4/49 (8%)
Adjusted *(c)*	18.0%	33.3%	11.7%
Terminal *(d)*	5/36 (14%)	7/32 (22%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.329N	P=0.071	P=0.336N
Incidental Tumor Test	P=0.275N	P=0.162	P=0.462N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.205N	P=0.124	P=0.238N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	16/50 (32%)	15/50 (30%)	11/50 (22%)
Adjusted *(c)*	39.7%	40.8%	33.3%
Terminal *(d)*	14/38 (37%)	12/33 (36%)	11/33 (33%)
Statistical Tests *(e)*			
Life Table	P=0.293N	P=0.483	P=0.322N
Incidental Tumor Test	P=0.260N	P=0.580N	P=0.376N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.158N	P=0.500N	P=0.184N
Adrenal: Pheochromocytoma or Malignant Pheochromocytoma			
Tumor Rates			
Overall *(b)*	17/50 (34%)	15/50 (30%)	11/50 (22%)
Adjusted *(c)*	41.1%	40.8%	33.3%
Terminal *(d)*	14/38 (37%)	12/33 (36%)	11/33 (33%)
Statistical Tests *(e)*			
Life Table	P=0.231N	P=0.557	P=0.258N
Incidental Tumor Test	P=0.213N	P=0.505N	P=0.330N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.113N	P=0.415N	P=0.133N
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	6/48 (13%)	10/50 (20%)	5/50 (10%)
Adjusted *(c)*	16.7%	29.1%	14.6%
Terminal *(d)*	6/36 (17%)	9/33 (27%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.511N	P=0.151	P=0.570N
Incidental Tumor Test	P=0.470N	P=0.194	P=0.614N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.400N	P=0.233	P=0.471N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	8/48 (17%)	11/50 (22%)	7/50 (14%)
Adjusted *(c)*	21.4%	30.7%	20.5%
Terminal *(d)*	7/36 (19%)	9/33 (27%)	6/33 (18%)
Statistical Tests *(e)*			
Life Table	P=0.530N	P=0.235	P=0.587N
Incidental Tumor Test	P=0.474N	P=0.348	P=0.560
Cochran-Armitage Trend, Fisher Exact Tests	P=0.404N	P=0.341	P=0.465N

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Pancreatic Islets: Islet-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/50 (4%)	1/49 (2%)
Adjusted *(c)*	7.9%	6.1%	3.0%
Terminal *(d)*	3/38 (8%)	2/33 (6%)	1/33 (3%)
Statistical Tests *(e)*			
Life Table	P=0.272N	P=0.564N	P=0.356N
Incidental Tumor Test	P=0.272N	P=0.564N	P=0.356N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.232N	P=0.500N	P=0.316N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	3/50 (6%)	3/50 (6%)
Adjusted *(c)*	7.4%	9.1%	9.1%
Terminal *(d)*	2/38 (5%)	3/33 (9%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.508	P=0.591	P=0.584
Incidental Tumor Test	P=0.474	P=0.584	P=0.533
Cochran-Armitage Trend, Fisher Exact Tests	P=0.586	P=0.661	P=0.661
Preputial Gland: Adenocarcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	1/50 (2%)	1/50 (2%)
Adjusted *(c)*	10.5%	3.0%	3.0%
Terminal *(d)*	4/38 (11%)	1/33 (3%)	1/33 (3%)
Statistical Tests *(e)*			
Life Table	P=0.137N	P=0.223N	P=0.223N
Incidental Tumor Test	P=0.137N	P=0.223N	P=0.223N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.108N	P=0.181N	P=0.181N
Preputial Gland: Carcinoma or Adenocarcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	2/50 (4%)	2/50 (4%)
Adjusted *(c)*	10.5%	6.1%	6.1%
Terminal *(d)*	4/38 (11%)	2/33 (6%)	2/33 (6%)
Statistical Tests *(e)*			
Life Table	P=0.316N	P=0.403N	P=0.403N
Incidental Tumor Test	P=0.316N	P=0.403N	P=0.403N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.260N	P=0.339N	P=0.339N
Testis: Interstitial-Cell Tumor			
Tumor Rates			
Overall *(b)*	45/50 (90%)	45/50 (90%)	49/49 (100%)
Adjusted *(c)*	97.8%	95.7%	100.0%
Terminal *(d)*	37/38 (97%)	31/33 (94%)	33/33 (100%)
Statistical Tests *(e)*			
Life Table	P=0.024	P=0.146	P=0.023
Incidental Tumor Test	P=0.066	P=0.596N	P=0.068
Cochran-Armitage Trend, Fisher Exact Tests	P=0.036	P=0.630	P=0.030

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the control. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Subcutaneous Tissue: Fibrosarcoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted *(c)*	0.0%	0.0%	8.1%
Terminal *(d)*	0/35 (0%)	0/31 (0%)	2/33 (6%)
Statistical Tests *(e)*			
Life Table	P=0.037	*(f)*	P=0.116
Incidental Tumor Test	P=0.028	*(f)*	P=0.094
Cochran-Armitage Trend, Fisher Exact Tests	P=0.036	*(f)*	P=0.121
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	1/50 (2%)	0/50 (0%)	3/50 (6%)
Adjusted *(c)*	2.9%	0.0%	7.4%
Terminal *(d)*	1/35 (3%)	0/31 (0%)	1/33 (3%)
Statistical Tests *(e)*			
Life Table	P=0.174	P=0.524N	P=0.301
Incidental Tumor Test	P=0.125	P=0.524N	P=0.223
Cochran-Armitage Trend, Fisher Exact Tests	P=0.171	P=0.500N	P=0.309
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	7/50 (14%)	9/50 (18%)	11/50 (22%)
Adjusted *(c)*	16.6%	23.8%	26.1%
Terminal *(d)*	3/35 (9%)	4/31 (13%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.192	P=0.318	P=0.219
Incidental Tumor Test	P=0.186	P=0.373	P=0.291
Cochran-Armitage Trend, Fisher Exact Tests	P=0.184	P=0.393	P=0.218
Hematopoietic System: All Leukemia			
Tumor Rates			
Overall *(b)*	7/50 (14%)	9/50 (18%)	12/50 (24%)
Adjusted *(c)*	16.6%	23.8%	28.6%
Terminal *(d)*	3/35 (9%)	4/31 (13%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.136	P=0.318	P=0.159
Incidental Tumor Test	P=0.124	P=0.373	P=0.210
Cochran-Armitage Trend, Fisher Exact Tests	P=0.125	P=0.393	P=0.154
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	8/50 (14%)	9/50 (18%)	14/50 (28%)
Adjusted *(c)*	19.2%	23.8%	31.6%
Terminal *(d)*	4/35 (11%)	4/31 (13%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.101	P=0.410	P=0.125
Incidental Tumor Test	P=0.096	P=0.479	P=0.206
Cochran-Armitage Trend, Fisher Exact Tests	P=0.087	P=0.500	P=0.114

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

Topography:Morphology	Vehicle Control	Low Dose	High Dose
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	17/49(35%)	10/50(20%)	13/50(26%)
Adjusted *(c)*	44.3%	29.8%	36.7%
Terminal *(d)*	13/34(38%)	8/31(26%)	11/33(33%)
Statistical Tests *(e)*			
Life Table	P=0.247N	P=0.145N	P=0.283N
Incidental Tumor Test	P=0.241N	P=0.139N	P=0.279N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.207N	P=0.078N	P=0.235N
Pituitary: Carcinoma			
Tumor Rates			
Overall *(b)*	0/49(0%)	3/50(6%)	2/50(4%)
Adjusted *(c)*	0.0%	9.7%	6.1%
Terminal *(d)*	0/34(0%)	3/31(10%)	2/33(6%)
Statistical Tests *(e)*			
Life Table	P=0.208	P=0.105	P=0.231
Incidental Tumor Test	P=0.208	P=0.105	P=0.231
Cochran-Armitage Trend, Fisher Exact Tests	P=0.219	P=0.125	P=0.253
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	17/49(35%)	13/50(26%)	15/50(30%)
Adjusted *(c)*	44.3%	38.9%	42.5%
Terminal *(d)*	13/34(38%)	11/31(35%)	13/33(39%)
Statistical Tests *(e)*			
Life Table	P=0.407N	P=0.360N	P=0.446N
Incidental Tumor Test	P=0.404N	P=0.359N	P=0.447N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.355N	P=0.235N	P=0.388N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	1/50(2%)	2/50(4%)	3/50(6%)
Adjusted *(c)*	2.3%	6.5%	9.1%
Terminal *(d)*	0/35(0%)	2/31(6%)	3/33(9%)
Statistical Tests *(e)*			
Life Table	P=0.216	P=0.464	P=0.293
Incidental Tumor Test	P=0.194	P=0.451	P=0.256
Cochran-Armitage Trend, Fisher Exact Tests	P=0.226	P=0.500	P=0.309
Adrenal: Pheochromocytoma and Malignant Pheochromocytoma			
Tumor Rates			
Overall *(b)*	2/50(4%)	2/50(4%)	3/50(6%)
Adjusted *(c)*	5.1%	6.5%	9.1%
Terminal *(d)*	1/35(3%)	2/31(6%)	3/33(9%)
Statistical Tests *(e)*			
Life Table	P=0.390	P=0.654	P=0.481
Incidental Tumor Test	P=0.364	P=0.644	P=0.442
Cochran-Armitage Trend, Fisher Exact Tests	P=0.408	P=0.691	P=0.500

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	10/50 (20%)	8/48 (17%)	6/50 (12%)
Adjusted *(c)*	28.6%	26.1%	18.2%
Terminal *(d)*	10/35 (29%)	7/29 (24%)	6/33 (18%)
Statistical Tests *(e)*			
Life Table	P=0.200N	P=0.570N	P=0.236N
Incidental Tumor Test	P=0.211N	P=0.574N	P=0.236N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.173N	P=0.435N	P=0.207N
Thyroid: C-Cell Carcinoma			
Tumor Rates			
Overall *(b)*	2/50 (4%)	2/48 (4%)	3/50 (6%)
Adjusted *(c)*	5.7%	6.9%	9.1%
Terminal *(d)*	2/35 (6%)	2/29 (7%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.385	P=0.626	P=0.473
Incidental Tumor Test	P=0.385	P=0.626	P=0.473
Cochran-Armitage Trend, Fisher Exact Tests	P=0.409	P=0.676	P=0.500
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	12/50 (24%)	10/48 (21%)	9/50 (18%)
Adjusted *(c)*	34.3%	32.8%	27.3%
Terminal *(d)*	12/35 (34%)	9/29 (31%)	9/33 (27%)
Statistical Tests *(e)*			
Life Table	P=0.314N	P=0.598	P=0.359N
Incidental Tumor Test	P=0.327N	P=0.595	P=0.359N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.272N	P=0.447N	P=0.312N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	8/50 (16%)	14/50 (28%)	11/50 (22%)
Adjusted *(c)*	21.8%	39.7%	30.7%
Terminal *(d)*	7/35 (20%)	11/31 (35%)	9/33 (27%)
Statistical Tests *(e)*			
Life Table	P=0.247	P=0.068	P=0.264
Incidental Tumor Test	P=0.246	P=0.115	P=0.246
Cochran-Armitage Trend, Fisher Exact Tests	P=0.285	P=0.114	P=0.306
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(b)*	14/50 (28%)	15/49 (31%)	16/50 (32%)
Adjusted *(c)*	38.9%	44.8%	42.4%
Terminal *(d)*	13/35 (37%)	13/31 (42%)	12/33 (36%)
Statistical Tests *(e)*			
Life Table	P=0.311	P=0.346	P=0.347
Incidental Tumor Test	P=0.374	P=0.420	P=0.400
Cochran-Armitage Trend, Fisher Exact Tests	P=0.375	P=0.474	P=0.414

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the control. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).
(f) No test was performed because there was no incidence in the low-dose or vehicle control group.

PRECHRONIC STUDIES

Single-Dose Study

Two of five males receiving 400 mg/kg and 4/5 males and 5/5 females receiving 800 mg/kg died (Table 8). The following average weight increases over the initial weight (on day 0) were calculated at the end of the 16th day for the surviving male and female mice:

Dose (mg/kg)	Weight Increase (Percent)	
	Males	Females
50	2	18
100	17	22
200	24	13
400	21	11
800	38	—

Male and female mice exhibited a transient, dose-related toxicity which was most marked in the 100, 200, 400, and 800 mg/kg groups. This included inactivity, drooping eyelids, and ruffled fur.

The peritoneal cavities were examined in male mice administered 200, 400, or 800 mg/kg and in female mice administered 100, 200, or 400 mg/kg. The lower third of the mucosal surface of the stomach was thickened and necrotic. The stomach adhered to the peritoneal wall in male mice administered 400 or 800 mg/kg and in female mice administered 200 or 400 mg/kg. The severity of these effects was dose related.

The highest dosage levels producing no deaths were 200 mg/kg in the males and 400 mg/kg in the females. In addition, the 100, 200, 400, and 800 mg/kg levels produced toxicity. For these reasons, the highest dose level in the 14-day study was set at 50 mg/kg.

Fourteen-Day Study

One male mouse administered 50 mg/kg died (Table 9). A thickened area of mucosa in the nonglandular region of the stomach was observed in 4/5 males and 5/5 females administered 50 mg/kg. A thickened urinary bladder wall was seen in 4/5 males and 1/5 females administered 50 mg/kg. The average weight gain in the experimental groups varied from 3% to 16%.

No other signs of toxicity were observed. Due to the stomach and bladder lesions observed at the 50 mg/kg dose, the highest dose set for the 13-week study was 25 mg/kg.

Thirteen-Week Study

No compound-related deaths or histopathologic effects in the stomach or other tissues were observed. Mean body weight gains of control and dosed groups were comparable (Table 10). The highest dose level (25 mg/kg) had no effect on male or female B6C3F1 mice.

Doses of 12 and 25 mg/kg allyl isothiocyanate, administered five times per week by gavage, were selected for mice in the chronic study because compound-related effects were observed in the 14-day study at 50 mg/kg.

TABLE 8. DOSAGE AND SURVIVAL OF MICE ADMINISTERED A SINGLE DOSE OF ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

Dose (mg/kg)	Survival *(a)*	
	Males	Females
50	5/5	5/5
100	5/5	5/5
200	5/5	5/5
400	3/5 *(b)*	5/5
800	1/5 *(c)*	0/5 *(d)*

(a) Number surviving/number initially in the group.
(b) Deaths occurred on days 1 and 14.
(c) Two animals died on day 1 and two animals on day 2.
(d) Four animals died on day 1 and one animal on day 2.

TABLE 9. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF MICE RECEIVING ALLYL ISOTHIOCYANATE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weight (grams)		
		Initial	Final	Change *(b)*
Males				
3	5/5	20.2 ± 0.4	21.0 ± 0.7	+0.8 ± 0.5
6	5/5	20.6 ± 0.2	22.6 ± 0.7	+2.0 ± 0.5
12	5/5	20.2 ± 0.7	21.0 ± 1.0	+0.8 ± 0.4
25	5/5	19.8 ± 0.5	21.8 ± 0.7	+2.0 ± 0.5
50	4/5 *(c)*	20.5 ± 0.7	23.8 ± 0.5	+3.3 ± 0.8
Females				
3	5/5	17.4 ± 0.4	19.0 ± 0.3	+1.6 ± 0.5
6	5/5	16.6 ± 0.2	18.8 ± 0.7	+2.2 ± 0.7
12	5/5	17.8 ± 0.5	18.4 ± 0.4	+0.6 ± 0.2
25	5/5	16.8 ± 0.4	18.4 ± 0.2	+1.6 ± 0.5
50	5/5	17.6 ± 0.5	18.0 ± 0.9	+0.4 ± 1.0

(a) Number surviving/number initially in the group. All calculations refer only to the survivors of each group.
(b) Mean weight change of the survivors of the group ± standard error of the mean.
(c) Death occurred on day 15, the day after administration of the test material was discontinued.

TABLE 10. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE FOR 13 WEEKS

Dose *(a)* (mg/kg)	Survival *(b)*	Mean Body Weight (grams)			Weight Change Relative to Controls *(d)* (Percent)
		Initial	Final	Change *(c)*	
Males					
0*(e)*	10/10	18.7 ±0.5	32.4 ±0.6	+13.7 ±0.5	
1.5	9/10 *(f)*	19.4 ±0.3	34.1 ±1.1	+14.7 ±1.1	+ 7.3
3	10/10	18.2 ±0.6	33.4 ±1.1	+15.2 ±0.8	+10.9
6	10/10	18.7 ±0.7	35.0 ±0.8	+16.3 ±0.8	+19.0
12	9/10 *(f)*	20.1 ±0.5	32.8 ±0.4	+12.7 ±0.4	- 7.3
25	10/10	19.9 ±0.4	35.2 ±0.6	+15.3 ±0.8	+11.7
Females					
0*(e)*	10/10	16.1 ±0.4	25.3 ±0.3	+9.2 ±0.4	
1.5	10/10	15.6 ±0.3	24.3 ±0.5	+8.7 ±0.7	- 5.4
3	8/10 *(f)*	16.4 ±0.5	24.5 ±0.6	+8.1 ±0.2	-12.0
6	9/10 *(f)*	16.6 ±0.4	25.2 ±0.6	+8.6 ±0.5	- 6.5
12	9/10 *(f)*	16.9 ±0.5	25.9 ±0.8	+9.0 ±0.7	- 2.2
25	10/10	15.9 ±0.4	24.5 ±0.5	+8.6 ±0.3	- 6.5

(a) Allyl isothiocyanate in corn oil was administered 5 days per week.
(b) Number surviving/number initially in the group. All calculations refer only to the survivors of each group.
(c) Mean weight change of the survivors of the group ± standard error of the mean.
(d) Weight change of the dosed group relative to that of the controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

(e) Vehicle controls received corn oil alone.
(f) Death was a result of gavage error.

CHRONIC STUDY

Body Weights and Clinical Signs

Throughout most of the study, mean body weights of high-dose male and female mice were higher than those of the vehicle controls (Figure 3, Appendix H, Table H2).

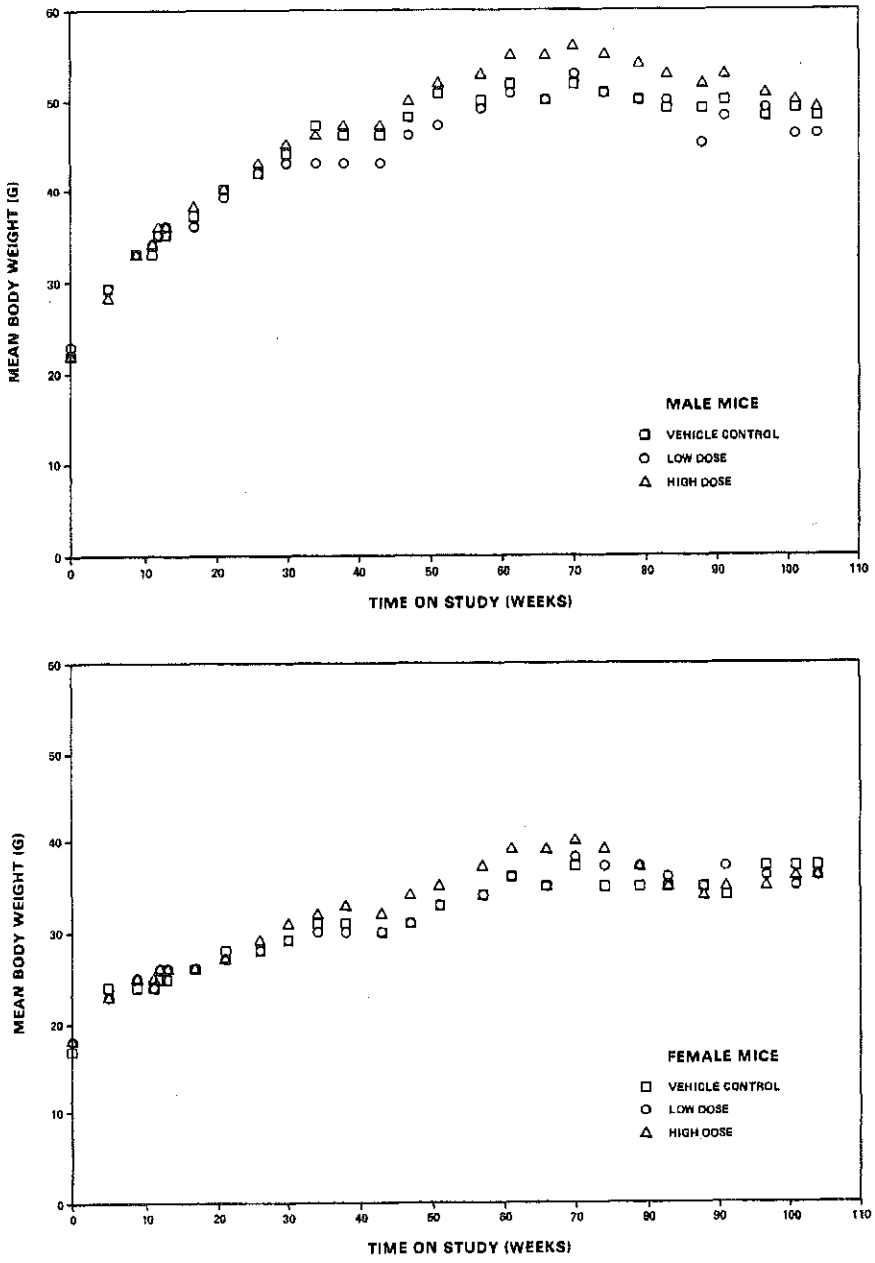

Figure 3. Growth Curves for Mice Administered Allyl Isothiocyanate by Gavage.

Survival

Estimates of the probabilities of survival of male and female mice administered allyl isothiocyanate by gavage at the doses of this bioassay, together with those of the control groups, are shown by the Kaplan and Meier curves in Figure 4. No significant differences in survival were observed between any groups of either sex. The survival in control female mice was consistently lower than the survival in either dosed group after week 40. One control male, one low-dose

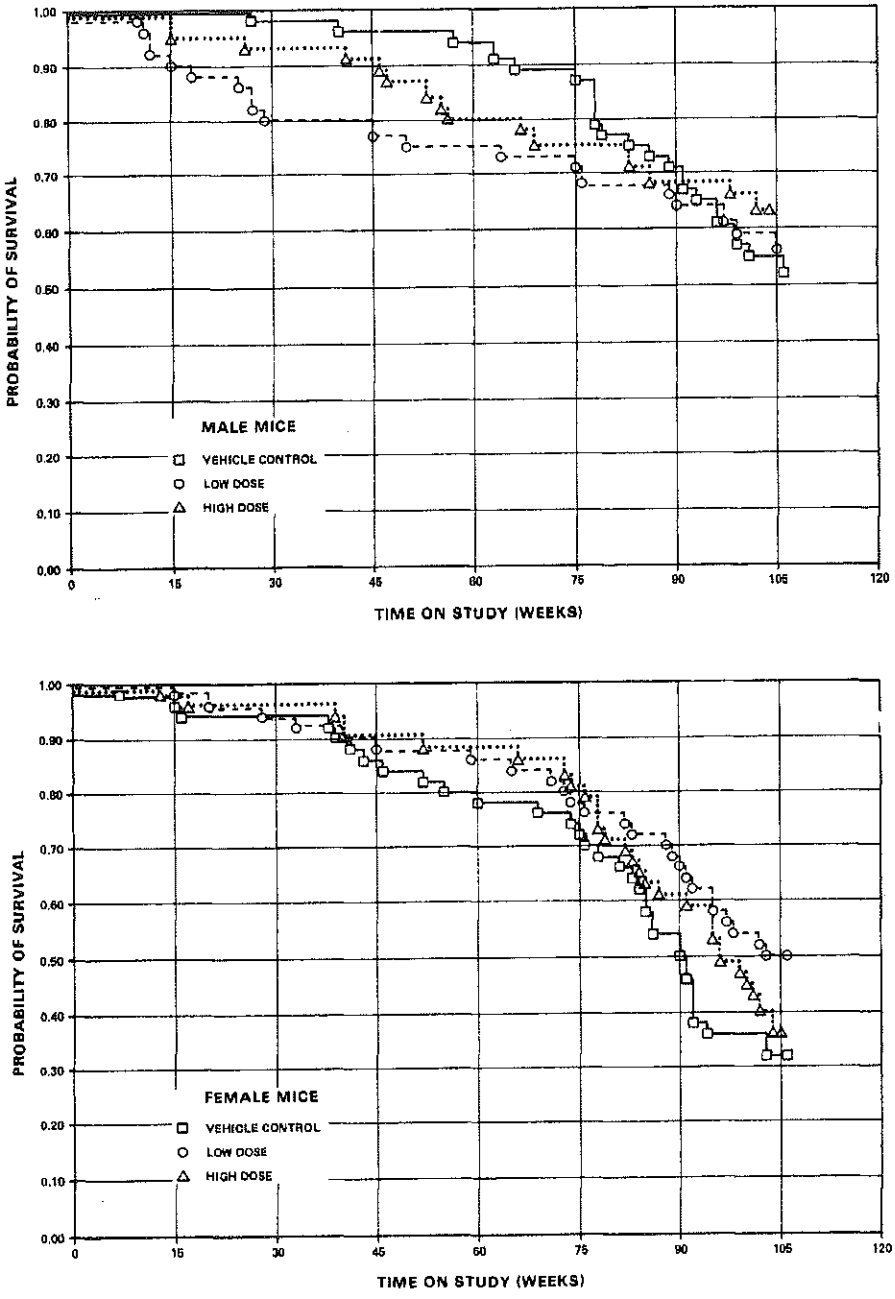

Figure 4. Survival Curves for Mice Administered Allyl Isothiocyanate by Gavage.

male, and two high-dose female mice died during weeks 104-106. In the statistical analyses reported in Tables I1 and 12, no distinction was made between these animals and those killed during this termination period. One control male (at week 41), six low-dose males (at weeks 42, 48, 56, 59, 60, and 65), seven high-dose males (at weeks 6, 20, 29, 31, 35, 62, and 65), and one high-dose female (at week 60) were accidentally killed (due to gavage error) during the study.

In male mice, 26/50 (52%) of the controls, 24/50 (48%) of the low-dose, and 27/50 (54%) of the high-dose group lived to the termination period of the study at 104-106 weeks. In female mice, 16/50 (32%) of the controls, 25/50 (50%) of the low-dose, and 18/50 (36%) of the high-dose group lived to the termination period of the study at 104-106 weeks. Suppurative inflammation of the peritoneum, uterus, or multiple organs was seen in many of the female mice that died before 104 weeks (13/34 controls, 6/25 low-dose, 12/30 high-dose). These lesions are suggestive of generalized infection and may have been causative in these early deaths.

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in mice are summarized in Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status for each individual animal in the male and female mouse studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2. Tables I1 and 12 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Liver: A significant, ($P<0.01$) dose-related increase in cytoplasmic vacuolization was observed in male mice (control 2/49, 4%; low-dose, 8/49, 16%; high-dose, 13/50, 26%). The distribution of these vacuoles was not consistent, but most livers had some centrilobular component. In other male mice with cytoplasmic vacuolization, the distribution was more consistently centrilobular. The vacuoles contained fat as determined by special stains of frozen sections. The degree of severity was similiar in the three groups.

TABLE 11. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma without Carcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	3/50 (6%)	4/50 (8%)
Adjusted *(c)*	14.8%	10.6%	14.3%
Terminal *(d)*	4/27 (15%)	2/25 (8%)	3/27 (11%)
Statistical Tests *(e)*			
Life Table	P=0.435	P=0.557N	P=0.643N
Incidental Tumor Test	P=0.509	P=0.547N	P=0.575
Cochran-Armitage Trend, Fisher Exact Tests	P=0.575	P=0.500N	P=0.643
Lung: Alveolar/Bronchiolar Carcinoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	1/50 (2%)	3/50 (6%)
Adjusted *(c)*	0.0%	4.0%	10.3%
Terminal *(d)*	0/27 (0%)	1/25 (4%)	2/27 (7%)
Statistical Tests *(e)*			
Life Table	P=0.060	P=0.485	P=0.113
Incidental Tumor Test	P=0.048	P=0.485	P=0.084
Cochran-Armitage Trend, Fisher Exact Tests	P=0.061	P=0.500	P=0.121
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	4/50 (8%)	7/50 (14%)
Adjusted *(c)*	14.8%	14.5%	23.9%
Terminal *(d)*	4/27 (15%)	3/25 (12%)	5/27 (19%)
Statistical Tests *(e)*			
Life Table	P=0.191	P=0.588	P=0.253
Incidental Tumor Test	P=0.143	P=0.598	P=0.176
Cochran-Armitage Trend, Fisher Exact Tests	P=0.201	P=0.643	P=0.262
Hematopoietic System: Lymphoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/50 (4%)	0/50 (0%)
Adjusted *(c)*	8.9%	7.7%	0.0%
Terminal *(d)*	1/27 (4%)	1/25 (4%)	0/27 (0%)
Statistical Tests *(e)*			
Life Table	P=0.104N	P=0.576N	P=0.148N
Incidental Tumor Test	P=0.175N	P=0.661	P=0.194N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.083N	P=0.500N	P=0.121N
Liver: Adenoma without Carcinoma			
Tumor Rates			
Overall *(b)*	8/49 (16%)	5/49 (10%)	9/50 (18%)
Adjusted *(c)*	28.0%	18.7%	31.3%
Terminal *(d)*	7/27 (26%)	4/25 (16%)	8/27 (30%)
Statistical Tests *(e)*			
Life Table	P=0.411	P=0.349N	P=0.482
Incidental Tumor Test	P=0.439	P=0.378N	P=0.540
Cochran-Armitage Trend, Fisher Exact Tests	P=0.453	P=0.276N	P=0.518

TABLE 11. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	13/49 (27%)	9/49 (18%)	10/50 (20%)
Adjusted *(c)*	35.3%	29.4%	35.7%
Terminal *(d)*	5/27 (19%)	5/25 (20%)	9/27 (33%)
Statistical Tests *(e)*			
Life Table	P=0.356N	P=0.408N	P=0.385N
Incidental Tumor Test	P=0.534N	P=0.580N	P=0.597
Cochran-Armitage Trend, Fisher Exact Tests	P=0.261N	P=0.234N	P=0.298N
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	21/49 (43%)	14/49 (29%)	19/50 (38%)
Adjusted *(c)*	57.2%	45.4%	65.2%
Terminal *(d)*	12/27 (44%)	9/25 (36%)	17/27 (63%)
Statistical Tests *(e)*			
Life Table	P=0.476N	P=0.259N	P=0.490N
Incidental Tumor Test	P=0.469	P=0.392N	P=0.529
Cochran-Armitage Trend, Fisher Exact Tests	P=0.362N	P=0.103N	P=0.387N
Thyroid: Follicular-Cell Adenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/45 (4%)	1/50 (2%)
Adjusted *(c)*	11.1%	7.2%	3.7%
Terminal *(d)*	3/27 (11%)	1/24 (4%)	1/27 (4%)
Statistical Tests *(e)*			
Life Table	P=0.242N	P=0.576N	P=0.303N
Incidental Tumor Test	P=0.236N	P=0.569N	P=0.303N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.228N	P=0.550N	P=0.309N
Harderian Gland: Adenoma or Cystadenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	1/50 (2%)	1/50 (2%)
Adjusted *(c)*	10.0%	4.0%	3.7%
Terminal *(d)*	2/27 (7%)	1/25 (4%)	1/27 (4%)
Statistical Tests *(e)*			
Life Table	P=0.224N	P=0.346N	P=0.325N
Incidental Tumor Test	P=0.258N	P=0.420N	P=0.366N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.210N	P=0.309N	P=0.309N

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

TABLE 12. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Carcinoma			
Tumor Rates			
Overall *(b)*	0/47 (0%)	2/49 (4%)	3/49 (6%)
Adjusted *(c)*	0.0%	7.1%	11.8%
Terminal *(d)*	0/16 (0%)	0/25 (0%)	1/20 (5%)
Statistical Tests *(e)*			
Life Table	P=0.119	P=0.337	P=0.194
Incidental Tumor Test	P=0.247	P=0.395	P=0.281
Cochran-Armitage Trend, Fisher Exact Tests	P=0.091	P=0.258	P=0.129
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	2/47 (4%)	2/49 (4%)	3/49 (6%)
Adjusted *(c)*	7.9%	7.1%	11.8%
Terminal *(d)*	0/16 (0%)	0/25 (0%)	1/20 (5%)
Statistical Tests *(e)*			
Life Table	P=0.510	P=0.559N	P=0.626
Incidental Tumor Test	P=0.594	P=0.697N	P=0.600
Cochran-Armitage Trend, Fisher Exact Tests	P=0.425	P=0.676N	P=0.520
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/50 (4%)	1/49 (2%)
Adjusted *(c)*	13.6%	5.8%	5.0%
Terminal *(d)*	1/16 (6%)	0/25 (0%)	1/20 (5%)
Statistical Tests *(e)*			
Life Table	P=0.166N	P=0.354N	P=0.241N
Incidental Tumor Test	P=0.277N	P=0.604N	P=0.397N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.232N	P=0.500N	P=0.316N
Hematopoietic System: Lymphoma			
Tumor Rates			
Overall *(b)*	5/50 (10%)	4/50 (8%)	4/49 (8%)
Adjusted *(c)*	21.3%	11.7%	17.9%
Terminal *(d)*	1/16 (6%)	1/25 (4%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.326N	P=0.320N	P=0.375N
Incidental Tumor Test	P=0.393N	P=0.562N	P=0.448N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.447N	P=0.500N	P=0.513N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	5/50 (10%)	4/50 (8%)	6/49 (12%)
Adjusted *(c)*	21.3%	11.7%	24.6%
Terminal *(d)*	1/16 (6%)	1/25 (4%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.559	P=0.320N	P=0.593N
Incidental Tumor Test	P=0.559	P=0.562N	P=0.589N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.418	P=0.500N	P=0.486

TABLE 12. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	2/50 (4%)	3/49 (6%)	1/49 (2%)
Adjusted *(c)*	12.5%	10.9%	2.9%
Terminal *(d)*	2/16 (13%)	2/25 (8%)	0/20 (0%)
Statistical Tests *(e)*			
Life Table	P=0.325N	P=0.675N	P=0.445N
Incidental Tumor Test	P=0.453N	P=0.597	P=0.534N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.404N	P=0.490	P=0.508N
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	3/47 (6%)	3/45 (7%)	4/44 (9%)
Adjusted *(c)*	18.8%	11.0%	17.9%
Terminal *(d)*	3/16 (19%)	2/25 (8%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.535	P=0.465N	P=0.643
Incidental Tumor Test	P=0.493	P=0.561N	P=0.635N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.388	P=0.641	P=0.463
Pituitary: Carcinoma			
Tumor Rates			
Overall *(b)*	3/47 (6%)	3/45 (7%)	0/44 (0%)
Adjusted *(c)*	18.8%	12.0%	0.0%
Terminal *(d)*	3/16 (19%)	3/25 (12%)	0/20 (0%)
Statistical Tests *(e)*			
Life Table	P=0.054N	P=0.444N	P=0.081N
Incidental Tumor Test	P=0.054N	P=0.444N	P=0.081N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.112N	P=0.641	P=0.133N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	6/47 (13%)	6/45 (13%)	4/44 (9%)
Adjusted *(c)*	37.5%	22.6%	17.9%
Terminal *(d)*	6/16 (38%)	5/25 (20%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.176N	P=0.304N	P=0.212N
Incidental Tumor Test	P=0.200N	P=0.371N	P=0.183N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.354N	P=0.589	P=0.413N
Thyroid: Follicular-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	1/48 (2%)	3/47 (6%)	3/47 (6%)
Adjusted *(c)*	6.3%	12.5%	15.0%
Terminal *(d)*	1/16 (6%)	3/24 (12%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.302	P=0.458	P=0.385
Incidental Tumor Test	P=0.302	P=0.458	P=0.385
Cochran-Armitage Trend, Fisher Exact Tests	P=0.238	P=0.300	P=0.300

TABLE 12. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

A 2-year carcinogenesis bioassay of allyl isothiocyanate was conducted in F344/N rats and B6C3F1 mice. Doses of 12 or 25 mg/kg allyl isothiocyanate, administered 5 times per week by gavage, were selected for the chronic study since the 50 mg/kg dose administered in the 14-day study produced thickening of the mucosal surface of the stomach in male and female rats and mice, adherence of the stomach to the peritoneum in male rats, and a thickened urinary bladder wall in male mice. A dose of 25 mg/kg produced no gross lesions when administered for 14 consecutive days or when administered 5 times per week for 13 weeks, and all animals survived this dose.

Survival of dosed and control rats was comparable in the chronic study. Throughout the study, the mean body weights of high-dose male rats were lower than those of controls, and during the last half of the study the mean body weights of high-dose female rats were higher than the control values.

Transitional-cell papillomas of the urinary bladder occurred in dosed male rats with a statistically significant positive trend ($P<0.05$; incidence: control, 0/49, 0%; low-dose, 2/49, 4%; high-dose, 4/49, 8%). This benign urinary bladder tumor has not been observed among 568 untreated male control F344/N rats at this laboratory. The incidence of transitional-cell papillomas in male vehicle control rats in all laboratories in the NCI/NTP Bioassay Program is 1/994 (0.1%).

Epithelial hyperplasia was also seen at an increased incidence ($P<0.05$) in the urinary bladder of dosed male rats (control, 0/49, 0%; low-dose, 1/49, 2%; high-dose, 6/49, 12%). This hyperplasia did not occur in the animals that had transitional-cell papillomas. No urinary bladder calculi were seen in male rats.

Fibrosarcomas of the subcutaneous tissue occurred in female rats with a statistically significant positive trend ($P<0.05$; incidence: control, 0/50, 0%; low-dose, 0/50, 0%; high-dose, 3/50, 6%). The incidence in the high-dose group was not significant in comparison with the control group, and the evidence for the association of fibrosarcomas with administration of allyl isothiocyanate is considered equivocal. This tumor has been observed in 1/591 (0.2%) of the untreated female control F344/N rats at this laboratory and in 9/999 (0.9%) of the female vehicle control rats in all laboratories in the NCI/NTP Bioassay Program.

Retinopathy and cataract formation occurred at increased incidence in high-dose male rats and in low-dose female rats. This eye toxicity occurred most frequently in animals placed at the top of the racks, a position that gives maximum light exposure. Other chemicals assayed in a similar manner, such as stannous chloride (NTP, 1982), also showed a correlation between eye toxicity and rack position. However, not all NTP bioassays have shown a correlation between rack placement and eye toxicity. From these incidental observations it is not possible to determine whether a causative relationship exists for light exposure, allyl isothiocyanate administration, and eye defects.

Leukemia occurred in dosed male rats with a statistically significant positive trend ($P<0.05$; incidence: control, 2/50, 4%; low-dose, 6/50, 12%; high-dose, 8/50, 16%). The incidence in the high-dose group was significantly higher than that in the controls ($P<0.05$). However, this observed incidence was not statistically different from the historical incidence in male gavage controls in all laboratories in the Bioassay Program (96/999, 10%). No significant increases were observed for leukemia in female rats (7/50, 9/50, 12/50), or for lymphoma in male and female mice. Consequently, this increase is not considered to be the result of allyl isothiocyanate administration.

Survival of control and dosed female mice was comparable but lower than that usually seen at this laboratory, and the decreased survival may have reduced the incidence of late-appearing tumors in these groups. Suppurative inflammation of the peritoneum, uterus, or multiple organs was found in about one third of the female mice that died before the terminal kill, suggesting that an infection may have been a contributing factor to the decreased survival. Mean body weights of high-dose male and female mice were higher than those of controls throughout most of the study, and the animals may have been able to tolerate higher doses of allyl isothiocyanate.

The incidences of liver tumors in dosed male and female mice were not statistically significant. However, cytoplasmic vacuolization in the liver of dosed male mice was related to administration of allyl isothiocyanate (controls, 2/49, 4%; low-dose, 8/49, 16%; high-dose, 13/50, 26%).

The mechanism of action of allyl isothiocyanate is not known. Other unsaturated compounds, such as haloolefins, are thought to be metabolized *in vivo* to active epoxides (Eder et al., 1980). It

has been suggested that some haloolefins containing an allylic group may act as alkylating agents (Eder et al., 1980). Thiocyanate, which may be metabolically derived from isothiocyanate (White et al., 1978), has been shown to promote nitrosation of amines (Edwards et al., 1979; Fan and Tannenbaum, 1973). Isothiocyanates can react with an alcohol or an amine to give a thiocarbamate or thiourea (March, 1977). It is not known if any of these reactions were involved in producing the "ultimate carcinogen." An alternative mechanism of action for allyl isothiocyanate is as a promoter (Pitot and Sirica, 1980). Allyl isothiocyanate might enhance or stimulate the neoplastic growth of cells already initiated in the bladder cells, rather than initiate the first alteration itself. Allyl isothiocyanate was not mutagenic with or without activation in the Ames assay using strains TA 98, 100, 1535, and 1537 (NTP, 1981).

Other studies have shown that allyl isothiocyanate increases urine excretion (Muztar et al., 1979b). Williams (1974) has shown that allyl isothiocyanate and other isothiocyanates are directly toxic to cells grown in culture. These other toxic effects of allyl isothiocyanate were not measured in this bioassay. Whether they have an association with the carcinogenic effect observed in this study is not known.

Conclusions: Under the conditions of this bioassay, allyl isothiocyanate was carcinogenic for male F344/N rats, causing transitional-cell papillomas of the urinary bladder. Evidence for associating allyl isothiocyanate with subcutaneous fibrosarcomas in female F344/N rats was equivocal. Allyl isothiocyanate was not carcinogenic for B6C3F1 mice of either sex.

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
PAPILLOMA, NOS			1 (2%)
SQUAMOUS CELL PAPILLOMA	3 (6%)		4 (8%)
SQUAMOUS CELL CARCINOMA	1 (2%)		2 (4%)
BASAL-CELL TUMOR	1 (2%)		
BASAL-CELL CARCINOMA		1 (2%)	
ADNEXAL ADENOMA	1 (2%)		
KERATOACANTHOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS	1 (2%)	3 (6%)	1 (2%)
FIBROMA	2 (4%)	2 (4%)	2 (4%)
FIBROSARCOMA	5 (10%)	5 (10%)	1 (2%)
FIBROUS HISTIOCYTOMA, MALIGNANT	1 (2%)	2 (4%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(49)	(48)
SQUAMOUS CELL CARCINOMA, UNC PRI			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	2 (4%)	1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		2 (4%)
SARCOMA, NOS, UNC PRIM OR META			1 (2%)
FIBROSARCOMA, METASTATIC		1 (2%)	
FIBROUS HISTIOCYTOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
UNDIFFERENTIATED LEUKEMIA	2 (4%)	6 (12%)	8 (16%)
#SPLEEN	(50)	(49)	(50)
HISTIOCYTOMA, METASTATIC		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(49)	(50)
HEMANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	2 (4%)		5 (10%)
#PANCREAS	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)		
#DUODENUM	(48)	(49)	(47)
MUCINOUS ADENOCARCINOMA			1 (2%)
#ILEUM	(48)	(49)	(47)
OSTEOSARCOMA			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
TUBULAR-CELL ADENOMA		1 (2%)	
#URINARY BLADDER	(49)	(49)	(49)
TRANSITIONAL-CELL PAPILLOMA		2 (4%)	4 (8%)
LIPOMA		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(49)	(49)
CARCINOMA,NOS		1 (2%)	
ADENOMA, NOS	7 (15%)	12 (24%)	4 (8%)
#ADRENAL	(50)	(50)	(50)
CORTICAL ADENOMA	1 (2%)		
PHEOCHROMOCYTOMA	16 (32%)	15 (30%)	11 (22%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)	1 (2%)	
GANGLIONEUROMA		1 (2%)	
#THYROID	(48)	(50)	(50)
FOLLICULAR-CELL CARCINOMA	1 (2%)		1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
C-CELL ADENOMA	6 (13%)	10 (20%)	5 (10%)
C-CELL CARCINOMA	2 (4%)	1 (2%)	2 (4%)
#PANCREATIC ISLETS	(50)	(50)	(49)
ISLET-CELL ADENOMA	2 (4%)	2 (4%)	1 (2%)
ISLET-CELL CARCINOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA	3 (6%)	3 (6%)	3 (6%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS		1 (2%)	1 (2%)
ADENOMA, NOS	4 (8%)	1 (2%)	1 (2%)
ADENOCARCINOMA, NOS		1 (2%)	
CYSTADENOMA, NOS			
#TESTIS	(50)	(50)	(49)
INTERSTITIAL-CELL TUMOR	45 (90%)	45 (90%)	49 (100%)
NERVOUS SYSTEM			
#BRAIN	(50)	(49)	(50)
GLIOMA, NOS			1 (2%)
ASTROCYTOMA	2 (4%)		
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
ADENOMA, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
OSTEOMA		1 (2%)	
BODY CAVITIES			
*THORAX	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, METASTA	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*ABDOMINAL WALL	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
*MESENTERY	(50)	(50)	(50)
MESOTHELIOMA, NOS		1 (2%)	
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS			1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, METASTA			1 (2%)
SARCOMA, NOS			1 (2%)
FIBROUS HISTIOCYTOMA, METASTATIC	1 (2%)		
MESOTHELIOMA, NOS		1 (2%)	
MESOTHELIOMA, MALIGNANT		1 (2%)	1 (2%)
TAIL			
OSTEOSARCOMA		1	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHS	3	4	7
MORIBUND SACRIFICE	10	13	9
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED		1	1
TERMINAL SACRIFICE	32	32	33
ANIMAL MISSING			

a INCLUDES AUTOLYZED ANIMALS

B NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	48	50	49
TOTAL PRIMARY TUMORS	114	128	118
TOTAL ANIMALS WITH BENIGN TUMORS	47	49	49
TOTAL BENIGN TUMORS	90	99	86
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	25	21
TOTAL MALIGNANT TUMORS	22	27	24
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	3	1
TOTAL SECONDARY TUMORS	2	3	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	2	6
TOTAL UNCERTAIN TUMORS	2	2	6
TOTAL AHIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			2
TOTAL UNCERTAIN TUMORS			2

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
BASAL-CELL TUMOR	1 (2%)		
SARCOMA, NOS			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS		2 (4%)	
FIBROMA			3 (6%)
FIBROSARCOMA	1 (2%)		
FIBROUS HISTIOCYTOMA, MALIGNANT		1 (2%)	
OSTEOSARCOMA			
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR ADENOMA			1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		2 (4%)
C-CELL CARCINOMA, METASTATIC	1 (2%)		
FIBROUS HISTIOCYTOMA, METASTATIC	1 (2%)		
CARCINOSARCOMA			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, UNDIFFER-TYPE			1 (2%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
LEUKEMIA,NOS			1 (2%)
UNDIFFERENTIATED LEUKEMIA	7 (14%)	9 (18%)	11 (22%)
#SPLEEN	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
*TONGUE	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
#SALIVARY GLAND	(50)	(50)	(48)
ADENOMA, NOS	1 (2%)		
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE			1 (2%)
FIBROUS HISTIOCYTOMA, METASTATIC	1 (2%)		
#PANCREAS	(49)	(49)	(50)
ADENOMA, NOS			1 (2%)
URINARY SYSTEM			
#URINARY BLADDER	(49)	(49)	(50)
TRANSITIONAL-CELL PAPILLOMA			1 (2%)
ENDOMETRIAL STROMAL SARCOMA, MET			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(50)	(50)
CARCINOMA,NOS		3 (6%)	2 (4%)
ADENOMA, NOS	17 (35%)	10 (20%)	13 (26%)
#ADRENAL	(50)	(50)	(50)
CORTICAL ADENOMA	2 (4%)	2 (4%)	2 (4%)
PHEOCHROMOCYTOMA	1 (2%)	2 (4%)	3 (6%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)		
GANGLIONEUROMA	1 (2%)		
#THYROID	(50)	(48)	(50)
FOLLICULAR-CELL CARCINOMA		1 (2%)	
C-CELL ADENOMA	10 (20%)	8 (17%)	6 (12%)
C-CELL CARCINOMA	2 (4%)	2 (4%)	3 (6%)
#PANCREATIC ISLETS	(49)	(49)	(50)
ISLET-CELL ADENOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)		2 (4%)
FIBROADENOMA	8 (16%)	14 (28%)	11 (22%)
*CLITORAL GLAND	(50)	(50)	(50)
ADENOMA, NOS		1 (2%)	
*VAGINA	(50)	(50)	(50)
SARCOMA, NOS			1 (2%)
FIBROMA			
#UTERUS	(50)	(49)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
LEIOMYOMA			1 (2%)
ENDOMETRIAL STROMAL POLYP	14 (28%)	15 (31%)	16 (32%)
ENDOMETRIAL STROMAL SARCOMA	1 (2%)		
#CERVIX UTERI	(50)	(49)	(50)
SARCOMA, NOS			
#OVARY	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)		
NERVOUS SYSTEM			
#CEREBRAL VENTRICLE	(50)	(50)	(50)
ASTROCYTOMA		1 (2%)	
#BRAIN	(50)	(50)	(50)
ASTROCYTOMA	1 (2%)		
#BRAIN/THALAMUS	(50)	(50)	(50)
GLIOMA, NOS			1 (2%)
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
BASAL-CELL CARCINOMA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(50)	(50)
LIPOMA	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

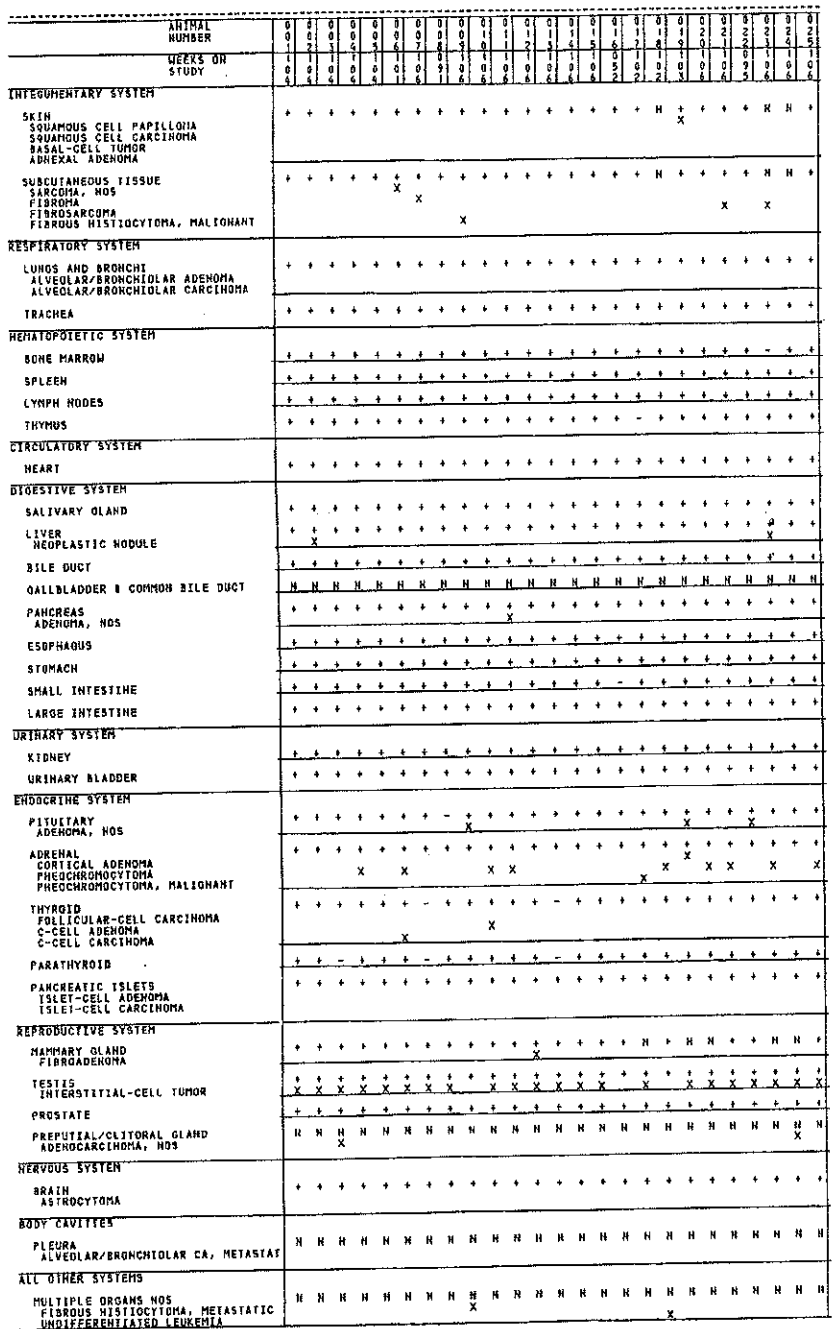
	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, INVASIV			1 (2%)
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITIOH SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHa	6	12	5
MORIBUND SACRIFICE	9	7	12
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED		2	
TERMINAL SACRIFICE	30	29	33
ANIMAL MISSING			
a INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	42	43	42
TOTAL PRIMARY TUMORS	77	72	86
TOTAL ANIMALS WITH BENIGN TUMORS	37	32	33
TOTAL BENIGN TUMORS	58	54	56
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	16	25
TOTAL MALIGNANT TUMORS	19	18	29
TOTAL ANIMALS WITH SECONDARY TUMORS#	2		1
TOTAL SECONDARY TUMORS	3		1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			1
TOTAL UNCERTAIN TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

VEHICLE CONTROL



+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	0261	0271	0281	0311	0312	0313	0314	0315	0316	0317	0318	0319	0321	0322	0323	0324	0325	0326	0327	0328	0329	0330	TOTAL TISSUES TUMORS
WEEKS ON STUDY	0 6	0 6	0 6	0 6	0 5	0 3	0 6	0 5	0 8	0 5	0 2	0 4	0 2	0 8	0 6	0 6	0 6	0 6	0 7	0 8	0 5	0 6	
INTEGUMENTARY SYSTEM																							
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	H	+	+	H	+	+	+	50
SQUAMOUS CELL PAPILLOMA																				X			3
SQUAMOUS CELL CARCINOMA	X																					X	1
BASAL-CELL TUMOR																			X				1
ADNEXAL ADENOMA																							1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	H	+	+	+	50
SARCOMA, NOS																							1
FIBROMA		X																					2
FIBROSARCOMA																			X				5
FIBROUS HISTIOCYTOMA, MALIGNANT	X																					X	1
RESPIRATORY SYSTEM																							
LUNGS AND BRONCHI	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA									X		X												2
ALVEOLAR/BRONCHIOLAR CARCINOMA																					X		1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																							
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CIRCULATORY SYSTEM																							
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																							
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEOPLASTIC NODULE																							2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	H	H	H	H	H	H	H	H	H	+	N	H	+	N	N	N	H	H	N	N	H	H	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																							1
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	48
URINARY SYSTEM	-																						
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																							
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	47
ADENOMA, NOS			X											X					X	X			7
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA					X		X				X		X			X				X			1
PHEOCHROMOCYTOMA	X			X		X																	16
PHEOCHROMOCYTOMA, MALIGNANT																							1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
FOLLICULAR-CELL CARCINOMA																	+						1
C-CELL ADENOMA			X		X				X							X	X		X			X	6
C-CELL CARCINOMA																							2
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	-	+	-	+	+	-	42
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA													X								X		2
ISLET-CELL CARCINOMA				X																			1
REPRODUCTIVE SYSTEM																							
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	H	+	+	+	+	+	+	+	50M
FIBROADENOMA																X	X						3
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	43
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	49
PREPUTIAL/CLITORAL GLAND	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	50M
ADENOCARCINOMA, NOS																				X		X	4
NERVOUS SYSTEM																							
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA							X										X						2
BODY CAVITIES																							
PLEURA	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	50M
ALVEOLAR/BRONCHIOLAR CA, METASTAT									X														1
ALL OTHER SYSTEMS																							
MULTIPLE ORGANS NOS	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	50M
FIBROUS HISTIOCYTOMA, METASTATIC																							1
UNDIFFERENTIATED LEUKEMIA								X															2

X ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
H: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3.

INDIVIDUAL ANIMAL T JMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUI Y OF ALLYL ISOTHIOCYANATE

LOW DOSE

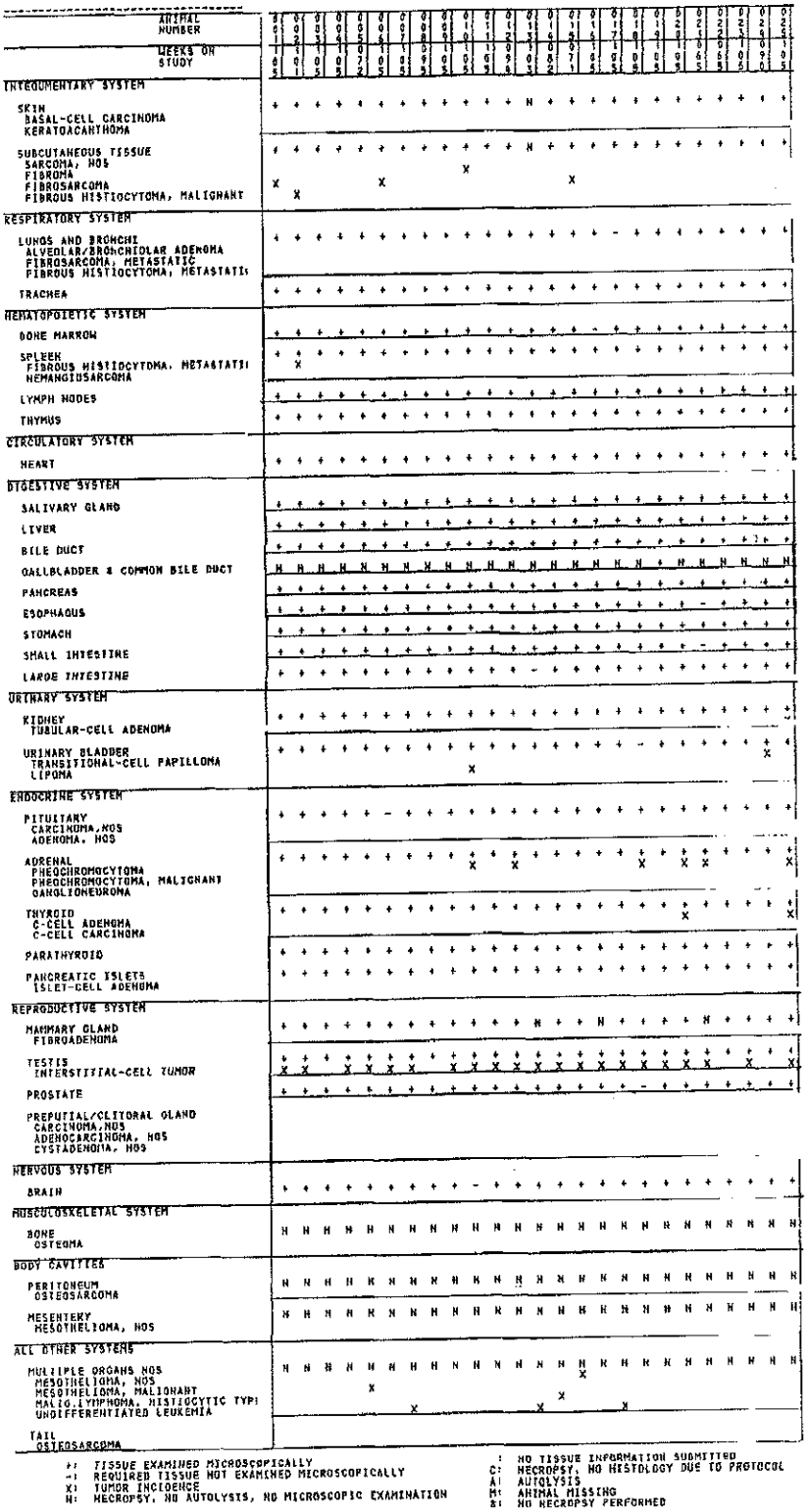
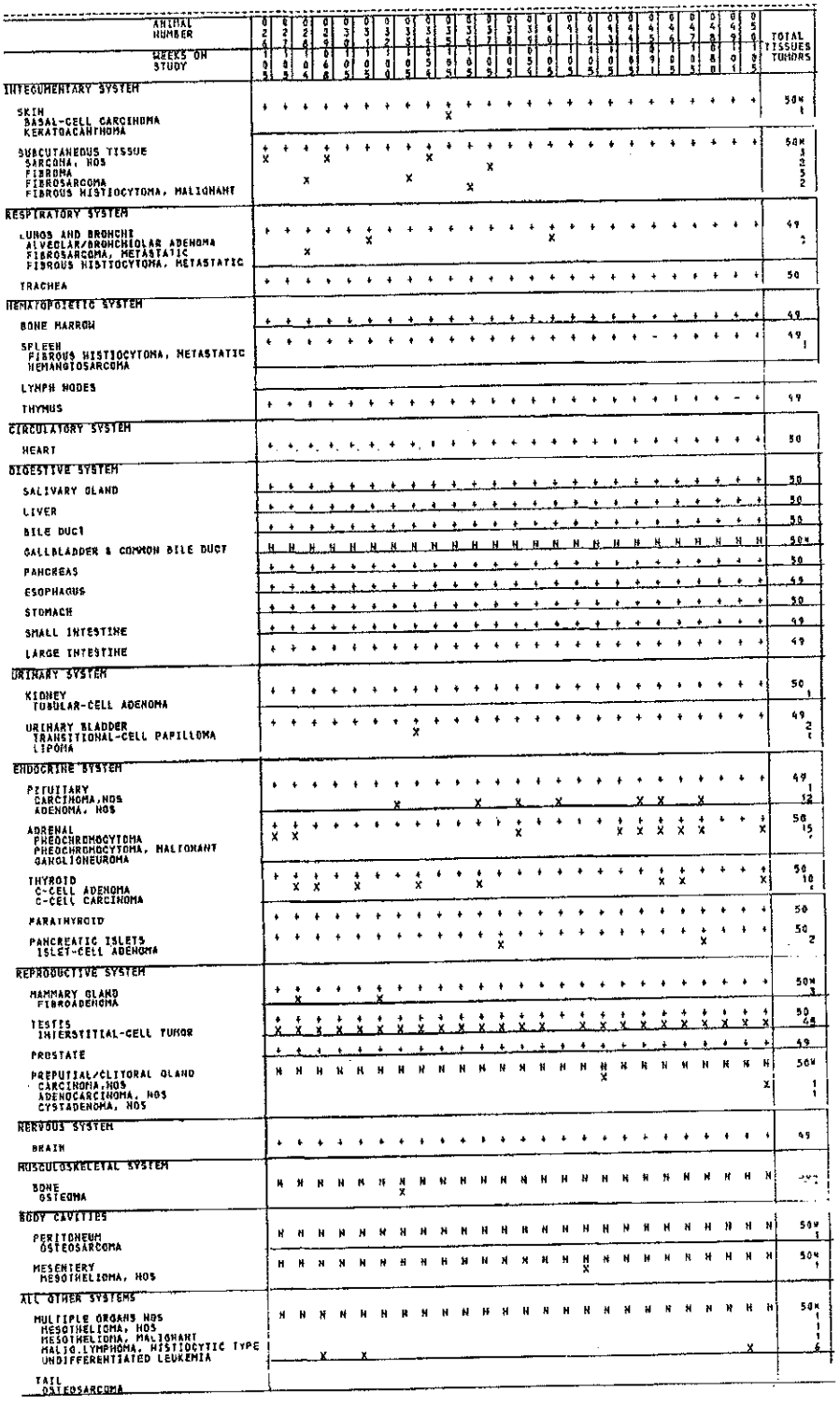


TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE



X ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
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A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE

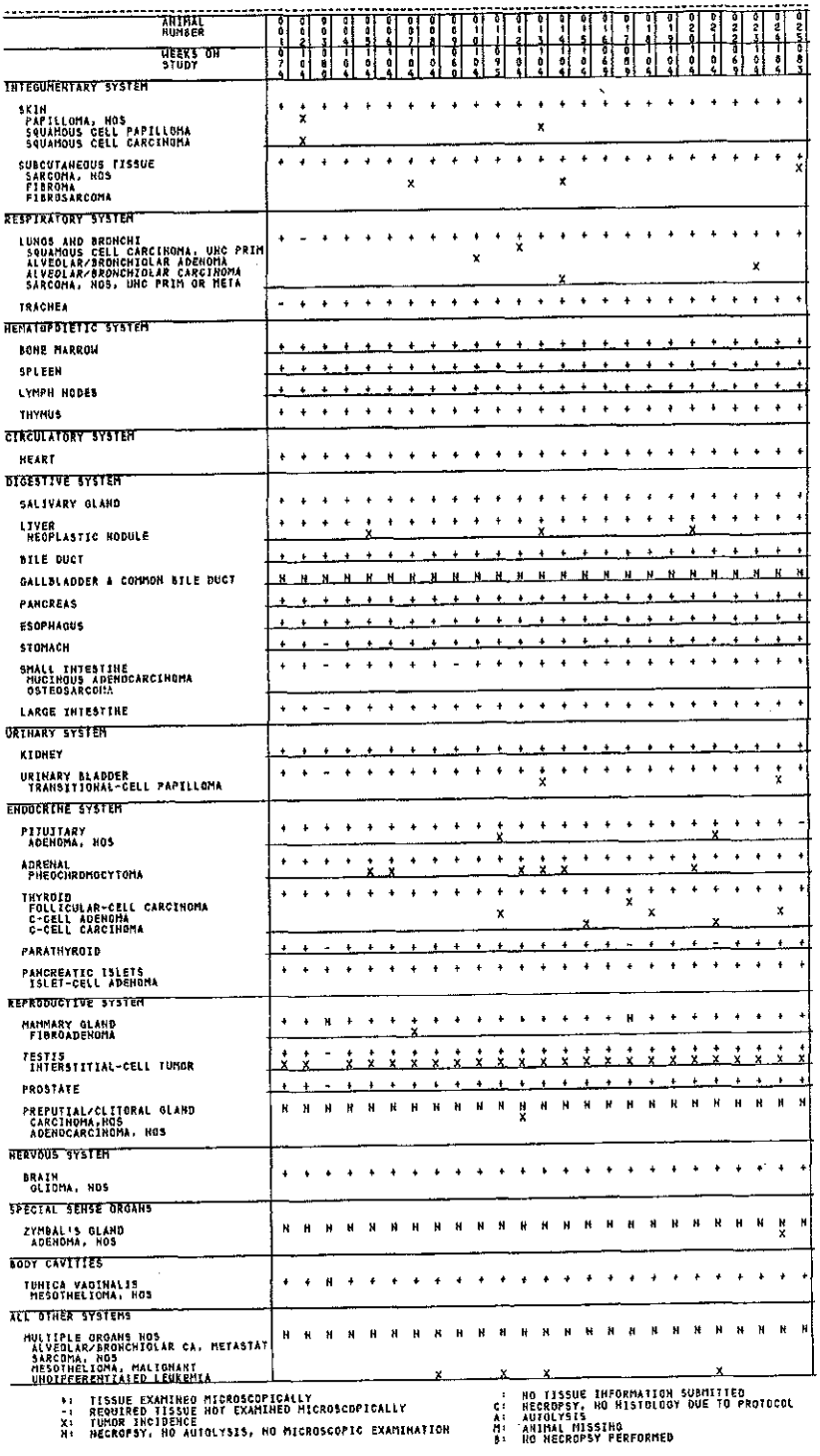

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES / TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50M
PAPILLOMA, NOS	1
SQUAMOUS CELL PAPILLOMA	4
SQUAMOUS CELL CARCINOMA	2
SUBCUTANEOUS TISSUE	50M
SARCOMA, NOS	1
FIBROMA	2
FIBROSARCOMA	1
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	48
SQUAMOUS CELL CARCINOMA, UNC PRIM	1
ALVEOLAR/BRONCHIOLAR ADENOMA	1
ALVEOLAR/BRONCHIOLAR CARCINOMA	2
SARCOMA, NOS, UNC PRIM OR META	1
TRACHEA	49
HEMATOPOIETIC SYSTEM	
BONE MARROW	50
SPLEEN	50
LYMPH NODES	50
THYMUS	49
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	50
LIVER	50
NEOPLASTIC NODULE	5
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	49
ESOPHAGUS	50
STOMACH	49
SMALL INTESTINE	47
MUCINOUS ADENOCARCINOMA	1
OSTEOSARCOMA	1
LARGE INTESTINE	49
URINARY SYSTEM	
KIDNEY	50
URINARY BLADDER	49
TRANSITIONAL-CELL PAPILLOMA	4
ENDOCRINE SYSTEM	
PITUITARY	49
ADENOMA, NOS	4
ADRENAL	50
PHEOCHROMOCYTOMA	11
THYROID	50
FOLLICULAR-CELL CARCINOMA	1
C-CELL ADENOMA	3
C-CELL CARCINOMA	2
PARATHYROID	45
PANCREATIC ISLETS	49
ISLET-CELL ADENOMA	1
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
FIBROADENOMA	3
TESTIS	49
INTERSTITIAL-CELL TUMOR	49
PROSTATE	49
PREPUTIAL/CLITORAL GLAND	50M
CARCINOMA,NOS	1
ADENOCARCINOMA, NOS	1
NERVOUS SYSTEM	
BRAIN	50
GLIOMA, NOS	1
SPECIAL SENSE ORGANS	
ZYMBAL'S GLAND	50M
ADENOMA, NOS	1
BODY CAVITIES	
TUNICA VAGINALIS	50M
MESOTHELIOMA, NOS	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
ALVEOLAR/BRONCHIOLAR CA, METASTAT	1
SARCOMA, NOS	1
MESOTHELIOMA, MALIGNANT	1
UNDIFFERENTIATED LEUKEMIA	4

\# ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
−: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
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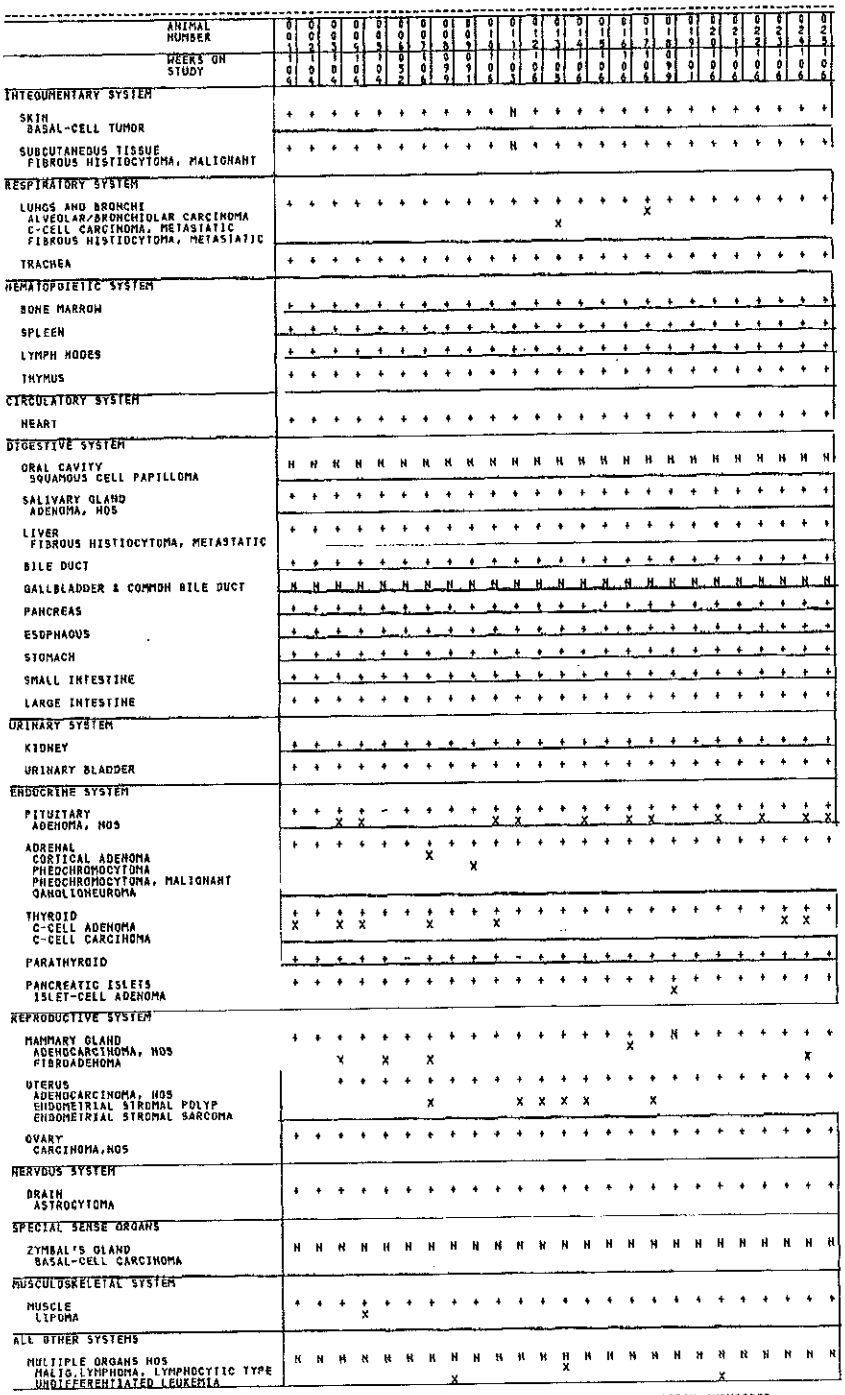
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

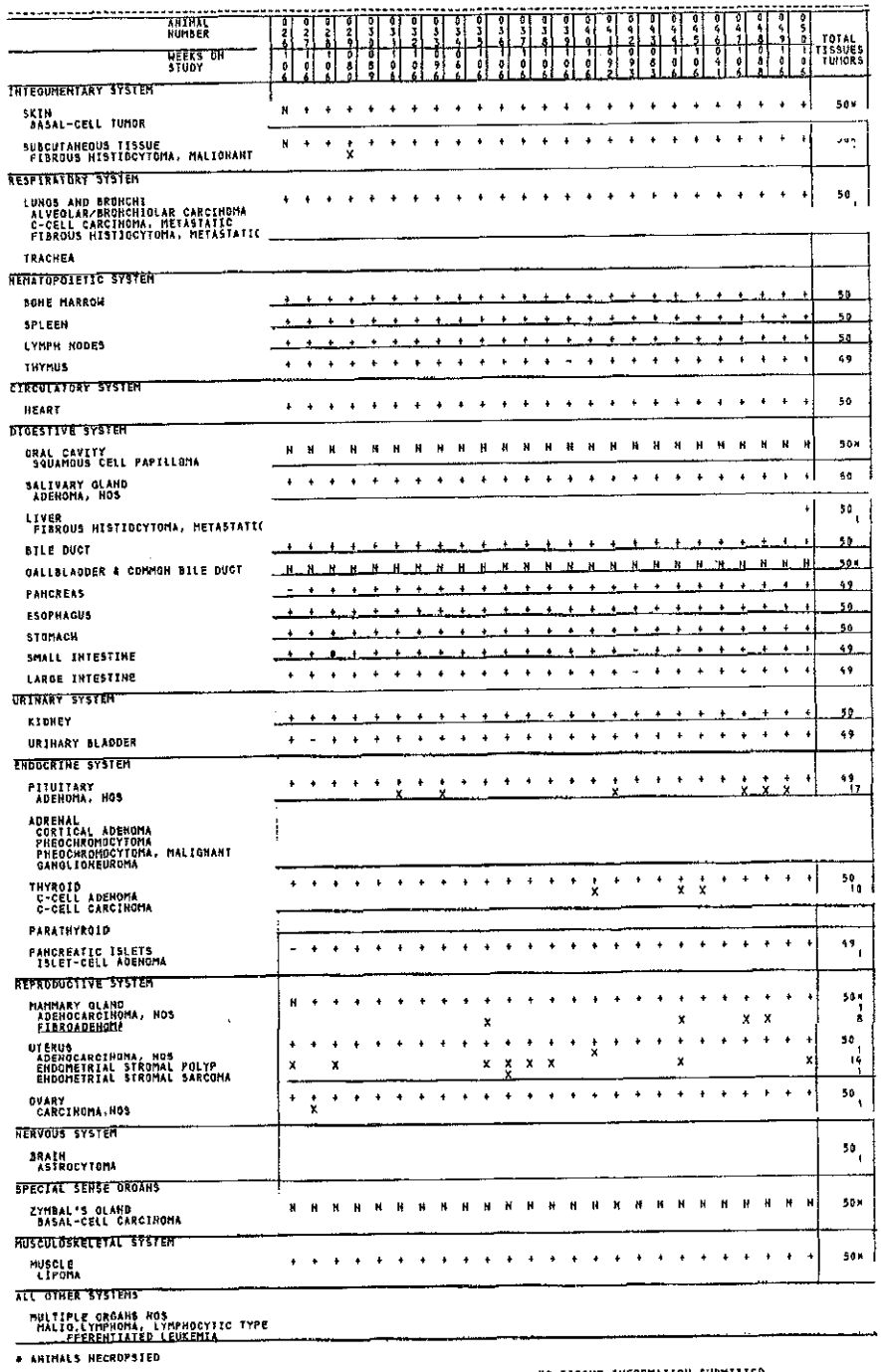
VEHICLE CONTROL



+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL



ANIMAL NUMBER	0 2 6 1 0 6	0 2 7 1 0 8	0 2 8 1 0 8	0 3 3 1 0 9	0 3 4 1 0 6	0 3 5 1 0 6	0 3 6 1 0 6	0 3 7 1 0 6	0 3 8 1 0 6	0 3 9 1 0 6	0 4 0 1 0 6	0 4 1 1 0 6	0 4 2 1 0 9	0 4 3 1 0 8	0 4 4 1 0 6	0 4 5 1 1 0	0 4 6 1 0 6	0 4 7 1 0 4	0 4 8 1 0 8	0 4 9 1 0 6	0 5 0 1 0 5	TOTAL TISSUES TUMORS
WEEKS ON STUDY																						
INTEGUMENTARY SYSTEM																						
SKIN	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
BASAL-CELL TUMOR																						
SUBCUTANEOUS TISSUE	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	[illegible]
FIBROUS HISTIOCYTOMA, MALIGNANT				X																		
RESPIRATORY SYSTEM																						
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR CARCINOMA																						1
C-CELL CARCINOMA, METASTATIC																						1
FIBROUS HISTIOCYTOMA, METASTATIC																						1
TRACHEA																						
HEMATOPOIETIC SYSTEM																						
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	49
CIRCULATORY SYSTEM																						
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																						
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL PAPILLOMA																						1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																						1
LIVER																					+	50
FIBROUS HISTIOCYTOMA, METASTATIC																						1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
URINARY SYSTEM																						
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																						
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS						X		X						X					X	X	X	17
ADRENAL																						
CORTICAL ADENOMA																						1
PHEOCHROMOCYTOMA																						1
PHEOCHROMOCYTOMA, MALIGNANT																						1
GANGLIONEUROMA																						1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA													X			X	X					10
C-CELL CARCINOMA																						1
PARATHYROID																						
PANCREATIC ISLETS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ISLET-CELL ADENOMA																						1
REPRODUCTIVE SYSTEM																						
MAMMARY GLAND	H	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
ADENOCARCINOMA, NOS											X					X			X	X		1
FIBROADENOMA																						8
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS	X		X								X	X	X	X					X		X	1
ENDOMETRIAL STROMAL POLYP												X				X						14
ENDOMETRIAL STROMAL SARCOMA																						1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS		X																				1
NERVOUS SYSTEM																						
BRAIN																						50
ASTROCYTOMA																						1
SPECIAL SENSE ORGANS																						
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N	50M
BASAL-CELL CARCINOMA																						1
MUSCULOSKELETAL SYSTEM																						
MUSCLE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
LIPOMA																						1
ALL OTHER SYSTEMS																						
MULTIPLE ORGANS NOS																						
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																						
DIFFERENTIATED LEUKEMIA																						

\# ANIMALS NECROPSIED

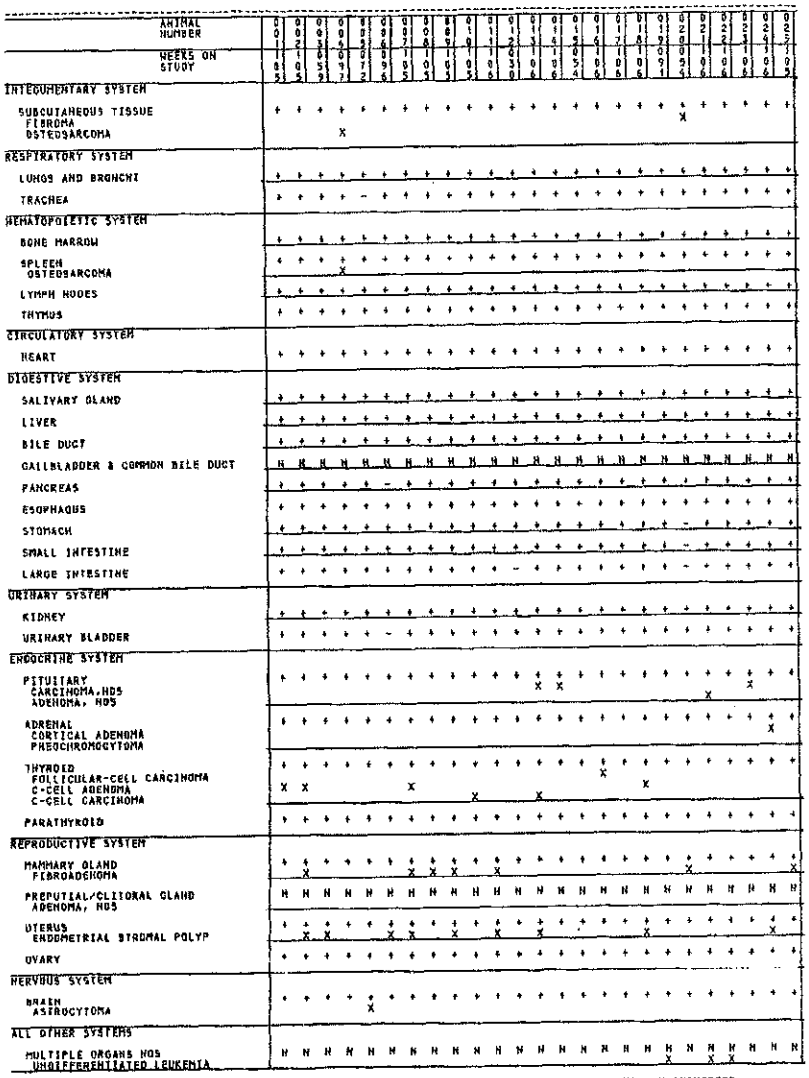
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

LOW DOSE



+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	0 2 6 7	0 2 7 8	0 2 8 9	0 3 0 1	0 3 1 2	0 3 3 3	0 3 4 4	0 3 5 5	0 3 6 6	0 3 7 7	0 3 7 8	0 3 8 9	0 4 0 0	0 4 1 2	0 4 2 3	0 4 3 5	0 4 4 6	0 4 4 7	0 4 4 8	0 4 5 0	TOTAL TISSUES TUMORS
WEEKS ON STUDY	0 9 7	0 9 1 1	1 0 5 1	1 0 6	1 0 5 4	0 7 7	0 5 6	1 0 6 1	0 9 0	0 6 1	0 6 5	0 6 6	1 0 6 3	1 0 7 6	1 0 6 6	1 0 6 1	1 0 9 1	0 9 4	0 6 6	0 6 6	0 6 8	0 9 5
INTEGUMENTARY SYSTEM																					
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	50M
FIBROMA					X																		6
OSTEOSARCOMA																							1
RESPIRATORY SYSTEM																							
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																							
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
OSTEOSARCOMA																							1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CIRCULATORY SYSTEM																							
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																							
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																							
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																							
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS																							3
ADENOMA, NOS	X		X					X			X	X			X	X	X	X					10
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA							X																2
PHEOCHROMOCYTOMA									X									X					2
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	48
FOLLICULAR-CELL CARCINOMA																							1
C-CELL ADENOMA		X							X			X						X					8
C-CELL CARCINOMA																							2
PARATHYROID	+	+	+	+	+	–	+	+	+	+	+	+	–	–	–	+	+	+	+	–	+	+	45
REPRODUCTIVE SYSTEM																							
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	50M
FIBROADENOMA						X					X	X	X					X	X			X	14
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS				X																			1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	49
ENDOMETRIAL STROMAL POLYP			X								X	X	X						X	X			15
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																							
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA																							1
ALL OTHER SYSTEMS																							
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
UNDIFFERENTIATED LEUKEMIA	X	X								X				X		X						X	9

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
–: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE

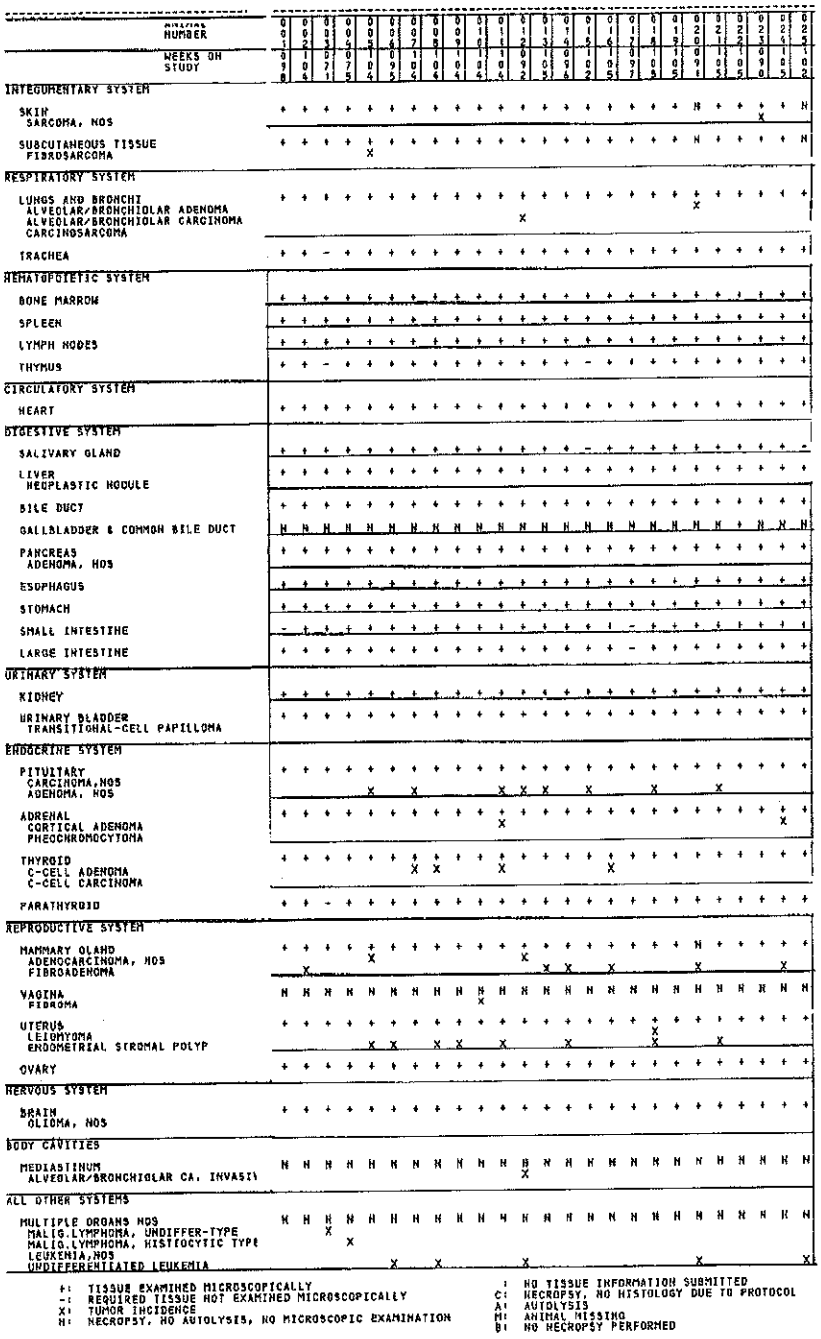


TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50*
SARCOMA, NOS	1
SUBCUTANEOUS TISSUE	50*
FIBROSARCOMA	3
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
ALVEOLAR/BRONCHIOLAR ADENOMA	1
ALVEOLAR/BRONCHIOLAR CARCINOMA	2
CARCINOSARCOMA	1
TRACHEA	49
HEMATOPOIETIC SYSTEM	
BONE MARROW	48
SPLEEN	50
LYMPH NODES	50
THYMUS	47
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	48
LIVER	50
NEOPLASTIC NODULE	1
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50*
PANCREAS	50
ADENOMA, NOS	1
ESOPHAGUS	50
STOMACH	50
SMALL INTESTINE	48
LARGE INTESTINE	49
URINARY SYSTEM	
KIDNEY	50
URINARY BLADDER	50
TRANSITIONAL-CELL PAPILLOMA	1
ENDOCRINE SYSTEM	
PITUITARY	50
CARCINOMA,NOS	2
ADENOMA, NOS	13
ADRENAL	50
CORTICAL ADENOMA	2
PHEOCHROMOCYTOMA	3
THYROID	50
C-CELL ADENOMA	6
C-CELL CARCINOMA	3
PARATHYROID	47
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50*
ADENOCARCINOMA, NOS	2
FIBROADENOMA	11
VAGINA	50*
FIBROMA	1
UTERUS	50
LEIOMYOMA	1
ENDOMETRIAL STROMAL POLYP	16
OVARY	50
NERVOUS SYSTEM	
BRAIN	50
GLIOMA, NOS	1
BODY CAVITIES	
MEDIASTINUM	50*
ALVEOLAR/BRONCHIOLAR CA, INVASIVE	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50*
MALIG.LYMPHOMA, UNDIFFER-TYPE	1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1
LEUKEMIA,NOS	1
UNDIFFERENTIATED LEUKEMIA	11

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
PAPILLOMA, NOS	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
HEPATOCELLULAR CARCINOMA, METAST	5 (10%)	2 (4%)	5 (10%)
ALVEOLAR/BRONCHIOLAR ADENOMA	4 (8%)	3 (6%)	3 (6%)
ALVEOLAR/BRONCHIOLAR CARCINOMA		1 (2%)	1 (2%)
SARCOMA, NOS, METASTATIC			
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2 (4%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)	2 (4%)	
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
HEMANGIOSARCOMA	1 (2%)		1 (2%)
#SPLEEN	(49)	(48)	(50)
HEMANGIOSARCOMA	1 (2%)	1 (2%)	1 (2%)
#MYOCARDIUM	(50)	(50)	(50)
HEMANGIOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(50)
BILE DUCT CARCINOMA			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEPATOCELLULAR ADENOMA	9 (18%)	6 (12%)	12 (24%)
HEPATOCELLULAR CARCINOMA	13 (27%)	9 (18%)	10 (20%)
MIXED HEPATO/CHOLANGIO CARCINOMA			1 (2%)
#STOMACH	(49)	(48)	(48)
SQUAMOUS CELL CARCINOMA			1 (2%)
#JEJUNUM	(45)	(42)	(45)
CARCINOMA,NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY/CORTEX	(49)	(49)	(50)
ADENOMA, NOS			
ENDOCRINE SYSTEM			
#ADRENAL	(47)	(49)	(50)
PHEOCHROMOCYTOMA			
#THYROID	(50)	(45)	(50)
FOLLICULAR-CELL ADENOMA	3 (6%)	2 (4%)	1 (2%)
REPRODUCTIVE SYSTEM			
NONE			
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS	2 (4%)	1 (2%)	1 (2%)
CYSTADENOMA, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
#MEDIASTINUM	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, INVASIV			
ALVEOLAR/BRONCHIOLAR CA, METASTA			1 (2%)
#MESENTERY	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)		
ALL OTHER SYSTEMS			
#MULTIPLE ORGANS	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
FIBROSARCOMA			1 (2%)
HEAD			
SARCOMA, NOS			1
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	14	17	10
MORIBUND SACRIFICE	9	3	6
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED	1	6	7
TERMINAL SACRIFICE	21	24	27
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

\# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	33	22	26
TOTAL PRIMARY TUMORS	39	27	39
TOTAL ANIMALS WITH BENIGN TUMORS	18	12	18
TOTAL BENIGN TUMORS	20	13	19
TOTAL ANIMALS WITH MALIGNANT TUMORS	18	14	17
TOTAL MALIGNANT TUMORS	18	14	20
TOTAL ANIMALS WITH SECONDARY TUMORS#	6	2	3
TOTAL SECONDARY TUMORS	6	2	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1		
TOTAL UNCERTAIN TUMORS	1		
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(49)
FIBROUS HISTIOCYTOMA, MALIGNANT			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(49)
MALIGNANT MELANOMA		1 (2%)	
FIBROUS HISTIOCYTOMA, MALIGNANT			1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(47)	(49)	(49)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	1 (2%)	
ALVEOLAR/BRONCHIOLAR CARCINOMA		2 (4%)	3 (6%)
OSTEOSARCOMA, METASTATIC			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)	1 (2%)	
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	3 (6%)	2 (4%)	1 (2%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		2 (4%)
MALIGNANT LYMPHOMA, MIXED TYPE			
LYMPHOCYTIC LEUKEMIA			1 (2%)
#SPLEEN	(47)	(48)	(49)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#MESENTERIC L. NODE	(50)	(47)	(49)
MALIGNANT LYMPHOMA, MIXED TYPE		1 (2%)	
#LIVER	(50)	(49)	(49)
KUPFFER-CELL SARCOMA			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
UNDIFFERENTIATED LEUKEMIA			1 (2%)
CIRCULATORY SYSTEM			
*SKIN	(50)	(50)	(49)
HEMANGIOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(49)
HEMANGIOSARCOMA	1 (2%)		
LYMPHANGIOMA			1 (2%)
#SPLEEN	(47)	(48)	(49)
HEMANGIOSARCOMA			1 (2%)
*MESENTERY	(50)	(50)	(49)
HEMANGIOMA		1 (2%)	
#UTERUS	(50)	(47)	(49)
HEMANGIOSARCOMA	1 (2%)		
#OVARY	(49)	(44)	(48)
HEMANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEPATOCELLULAR ADENOMA	2 (4%)	1 (2%)	
HEPATOCELLULAR CARCINOMA		2 (4%)	1 (2%)
#STOMACH	(47)	(47)	(49)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
SQUAMOUS CELL CARCINOMA			
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(45)	(44)
CARCINOMA,NOS	3 (6%)	3 (7%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ADENOMA, NOS	3 (6%)	3 (7%)	4 (9%)
ACIDOPHIL CARCINOMA	1 (2%)		
#THYROID	(48)	(47)	(47)
FOLLICULAR-CELL ADENOMA	1 (2%)	3 (6%)	1 (2%)
FOLLICULAR-CELL CARCINOMA			2 (4%)
#PANCREATIC ISLETS	(47)	(45)	(49)
ISLET-CELL ADENOMA		1 (2%)	
ISLET-CELL CARCINOMA			
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)		
ADENOCARCINOMA, NOS	1 (2%)	1 (2%)	1 (2%)
#UTERUS	(50)	(47)	(49)
SQUAMOUS CELL CARCINOMA			1 (2%)
ADENOCARCINOMA, NOS		1 (2%)	
ENDOMETRIAL STROMAL POLYP	2 (4%)		
#OVARY	(49)	(44)	(48)
TERATOMA, NOS			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
ACIDOPHIL CARCINOMA, INVASIVE	1 (2%)		
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)	1 (2%)	
CYSTADENOMA, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*FEMUR	(50)	(50)	(49)
OSTEOSARCOMA			1 (2%)
BODY CAVITIES			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	22	15	16
MORIBUND SACRIFICE	12	10	15
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED			1
TERMINAL SACRIFICE	11	25	18
ANIMAL MISSING			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	18	20	20
TOTAL PRIMARY TUMORS	25	28	26
TOTAL ANIMALS WITH BENIGN TUMORS	11	11	6
TOTAL BENIGN TUMORS	13	13	6
TOTAL ANIMALS WITH MALIGNANT TUMORS	10	14	15
TOTAL MALIGNANT TUMORS	12	15	19
TOTAL ANIMALS WITH SECONDARY TUMORS#	1		2
TOTAL SECONDARY TUMORS	1		2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			1
TOTAL UNCERTAIN TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

VEHICLE CONTROL

ANIMAL NUMBER	0 0 1 2	0 0 2 3	0 0 3 4	0 0 3 5	0 0 4 6	0 0 4 7	0 0 4 8	0 0 4 9	0 0 5 0	0 1 1 2	0 1 1 3	0 1 1 4	0 1 1 5	0 1 1 6	0 1 1 7	0 1 1 8	0 1 1 9	0 1 2 0	0 2 2 1	0 2 2 2	0 2 2 3	0 2 2 4	0 2 2 5
WEEKS ON STUDY	0 9 9	0 9 6	0 7 8	1 0 4	1 0 4	1 0 4	1 0 5	1 0 11	1 0 6	0 7 8	0 7 8	0 7 6	1 0 6	1 0 6	0 9 9	1 0 0	1 0 8	1 0 5	1 0 6	1 0 6	1 0 5	1 0 7	0 2 0 6
INTEGUMENTARY SYSTEM																							
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS								X															
RESPIRATORY SYSTEM																							
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA	X																			X	X		
ALVEOLAR/BRONCHIOLAR ADENOMA					X																		
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																							
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA										X													
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	-	-	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																							
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																							
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
HEPATOCELLULAR ADENOMA										X													X
HEPATOCELLULAR CARCINOMA	X	X	X		X										X					X	X		
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
GALLBLADDER & COMMON BILE DUCT	N	N	+	+	+	+	+	+	+	N	+	+	+	+	N	N	+	N	+	+	+	H	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
URINARY SYSTEM																							
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																							
PITUITARY	+	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA					X									X			X						
PARATHYROID	+	+	+	+	+	+	+	+	-	+	-	+	+	-	+	+	+	-	+	+	+	+	+
REPRODUCTIVE SYSTEM																							
MAMMARY GLAND	N	N	+	+	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	+	+
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																							
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																							
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																	X		X				
CYSTADENOMA, NOS																							
BODY CAVITIES																							
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS															X								
ALL OTHER SYSTEMS																							
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEPATOCELLULAR CARCINOMA, METASTA															X								
HEMANGIOSARCOMA																	X						
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																							
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																							

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES / TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50M
PAPILLOMA, NOS	1
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
HEPATOCELLULAR CARCINOMA, METASTA	5
ALVEOLAR/BRONCHIOLAR ADENOMA	4
TRACHEA	50
HEMATOPOIETIC SYSTEM	
BONE MARROW	50
SPLEEN	49
HEMANGIOSARCOMA	1
LYMPH NODES	50
THYMUS	41
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	50
LIVER	49
HEPATOCELLULAR ADENOMA	9
HEPATOCELLULAR CARCINOMA	13
BILE DUCT	49
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	47
ESOPHAGUS	50
STOMACH	49
SMALL INTESTINE	45
LARGE INTESTINE	45
URINARY SYSTEM	
KIDNEY	49
URINARY BLADDER	50
ENDOCRINE SYSTEM	
PITUITARY	46
ADRENAL	47
THYROID	50
FOLLICULAR-CELL ADENOMA	1
PARATHYROID	40
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
TESTIS	50
PROSTATE	50
NERVOUS SYSTEM	
BRAIN	50
SPECIAL SENSE ORGANS	
HARDERIAN GLAND	50M
ADENOMA, NOS	2
CYSTADENOMA, NOS	1
BODY CAVITIES	
MESENTERY	50M
MESOTHELIOMA, NOS	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
HEPATOCELLULAR CARCINOMA, METASTA	1
HEMANGIOSARCOMA	1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1

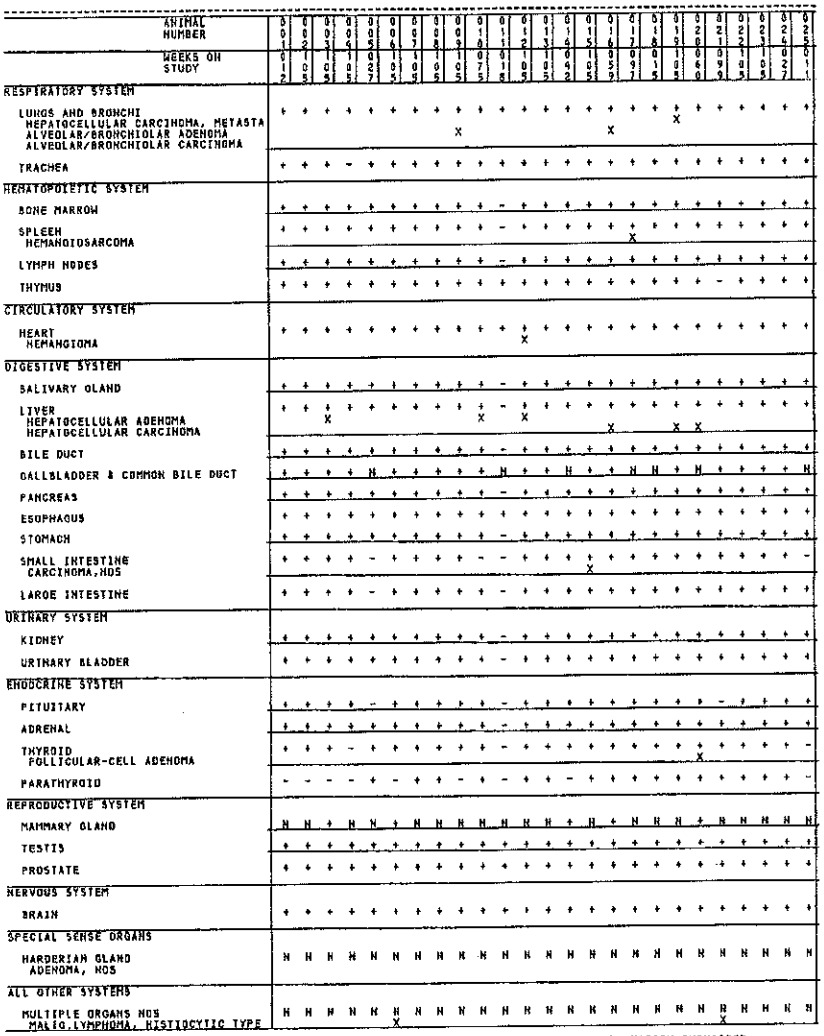
M ANIMALS NECROPSIED

A: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
M: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

LOW DOSE



ANIMAL NUMBER	0 0 1 2	0 0 2 5	0 0 3 5	0 0 4 5	0 0 5 5	0 0 6 5	0 0 7 5	0 0 8 5	0 0 9 5	0 1 0 5	0 1 1 5	0 1 2 5	0 1 3 5	0 1 4 5	0 1 5 5	0 1 6 5	0 1 7 5	0 1 8 5	0 1 9 5	0 2 0 5	0 2 1 5	0 2 2 5	0 2 3 5	0 2 4 5	0 2 5 5
WEEKS ON STUDY	0 1 2	0 0 5	0 0 5	0 0 5	1 0 2 7	0 0 5 1	1 0 0 9	0 0 6	0 0 5	0 0 7 5	0 1 0 8	0 1 0 5	0 1 0 5 1	0 1 0 4 2	0 1 0 5 1	0 1 0 5 9	0 0 9 7	0 1 0 5	0 1 0 5	0 1 0 6 0	0 0 9 9	0 1 0 5	0 0 9 5	0 1 0 2 7	0 1 0 1
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																			X						
ALVEOLAR/BRONCHIOLAR ADENOMA										X															
ALVEOLAR/BRONCHIOLAR CARCINOMA																X									
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																	X								
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA													X												
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA			X							X		X							X						
HEPATOCELLULAR CARCINOMA																X				X	X				
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	+	+	+	+	+	N	+	+	N	+	+	N	N	+	N	+	+	+	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-
CARCINOMA,NOS																X									
LARGE INTESTINE	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-
FOLLICULAR-CELL ADENOMA																				X					
PARATHYROID	-	-	-	-	+	-	+	+	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	+	N	N	+	N	N	N	N	N	N	N	+	N	+	N	N	N	+	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, HISTIOCYTIC TYPE						X															X				

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	0226	0227	0228	0230	0335	0336	0337	0339	0340	0341	0342	0343	0344	0345	0346	0347	0348	0349	0350	0351	0352	0353	0354	0355	0356	0357	0358	0359	0360	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1105	1076	0725	0805	0955	0956	0956	0954	0955	0952	0955	0955	0959	0959	0904	0964	0951	0910	0958	0958	0955	0955	0955	0955	0955	0955	0958	0955	0955	
RESPIRATORY SYSTEM																														
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA															X															2
ALVEOLAR/BRONCHIOLAR ADENOMA	X											X																		3
ALVEOLAR/BRONCHIOLAR CARCINOMA																														1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																														
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMANGIOSARCOMA																														1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CIRCULATORY SYSTEM																														
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOMA																														1
DIGESTIVE SYSTEM																														
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA					X																				X					6
HEPATOCELLULAR CARCINOMA								X					X		X					X				X					X	9
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	N	N	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	50M
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	42
CARCINOMA,NOS																														1
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																														
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																														
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYROID	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
FOLLICULAR-CELL ADENOMA																									X					2
PARATHYROID	+	+	-	-	+	+	-	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	36
REPRODUCTIVE SYSTEM																														
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	+	+	N	N	N	+	N	N	N	N	N	+	N	+	N	+	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																														
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																														
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																														1
ALL OTHER SYSTEMS																														
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																														2

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY; NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE

ANIMAL NUMBER	0001	0002	0003	0004	0005	0006	0007	0008	0009	0010	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025
WEEKS ON STUDY	104	104	105	062	041	045	105	064	064	064	045	061	104	035	061	049	053	063	065	047	069	053	104	104	106
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA										X															
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
SARCOMA, NOS, METASTATIC																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT CARCINOMA						X				X													X	X	X
HEPATOCELLULAR ADENOMA	X					X		X			X		X			X	X						X		
HEPATOCELLULAR CARCINOMA																									
MIXED HEPATO/CHOLANGIO CARCINOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	M	M	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
SMALL INTESTINE	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	+	-	+	+	-	-	-	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	+	M	M	+	M	M	M	M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
ADENOMA, NOS	X																								
BODY CAVITIES																									
MEDIASTINUM	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
ALVEOLAR/BRONCHIOLAR CA, METASTAT																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
SQUAMOUS CELL CARCINOMA, METASTAT																									
FIBROSARCOMA																									
HEMANGIOSARCOMA																									
HEAD NOS																									
SARCOMA, NOS																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
M: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES / TUMORS
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
ALVEOLAR/BRONCHIOLAR ADENOMA	5
ALVEOLAR/BRONCHIOLAR CARCINOMA	3
SARCOMA, NOS, METASTATIC	1
TRACHEA	49
HEMATOPOIETIC SYSTEM	
BONE MARROW	50
SPLEEN	50
HEMANGIOSARCOMA	1
LYMPH NODES	49
THYMUS	46
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	50
LIVER	50
BILE DUCT CARCINOMA	1
HEPATOCELLULAR ADENOMA	12
HEPATOCELLULAR CARCINOMA	10
MIXED HEPATO/CHOLANGIO CARCINOMA	1
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50#
PANCREAS	46
ESOPHAGUS	50
STOMACH	48
SQUAMOUS CELL CARCINOMA	1
SMALL INTESTINE	45
LARGE INTESTINE	47
URINARY SYSTEM	
KIDNEY	50
URINARY BLADDER	50
ENDOCRINE SYSTEM	
PITUITARY	46
ADRENAL	50
THYROID	50
FOLLICULAR-CELL ADENOMA	1
PARATHYROID	35
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50#
TESTIS	50
PROSTATE	50
NERVOUS SYSTEM	
BRAIN	50
SPECIAL SENSE ORGANS	
HARDERIAN GLAND	50#
ADENOMA, NOS	1
BODY CAVITIES	
MEDIASTINUM	50#
ALVEOLAR/BRONCHIOLAR CA, METASTAT	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50#
SQUAMOUS CELL CARCINOMA, METASTAT	1
FIBROSARCOMA	1
HEMANGIOSARCOMA	1
HEAD NOS	1
SARCOMA, NOS	

* ANIMALS NECROPSIED

A: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

VEHICLE CONTROL

ANIMAL NUMBER	0 0 1 1 0	0 0 1 2 4	0 0 1 3 1	0 0 1 4 1	0 0 1 5 4	0 0 1 6 4	0 0 1 7 A	0 0 1 8 4	0 0 1 8 3	0 0 1 8 5	0 0 1 9 1	0 0 1 9 6	0 1 1 2 0	0 1 1 2 1	0 1 1 3 9	0 1 1 5 6	0 1 1 5 9	0 1 1 6 7	0 1 1 7 6	0 1 1 8 6	0 1 1 9 9	0 1 2 0 2	0 1 2 2 1	0 2 2 2 3	0 2 2 3 6	0 2 2 5 3
WEEKS ON STUDY	0 0 6	0 0 6	0 0 4	0 4 1	0 0 4	1 0 4	0 7 A	0 8 4	0 8 3	0 8 1	0 7 5	0 4 6	0 9 0	0 5 9	0 6 9	0 8 0	0 8 7	0 0 6	1 0 6	0 0 6	0 3 8	0 9 2	0 0 6	1 0 3	0 1 5	0 5 3	1 0 3
INTEGUMENTARY SYSTEM																											
SUBCUTANEOUS TISSUE HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																											
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																											
BONE MARROW	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-
CIRCULATORY SYSTEM																											
HEART	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																											
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
LIVER HEPATOCELLULAR ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	H	+	+	+	H	+	H	+	+	+	H	+	+	+	+	+	+	+	+	+	H	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
URINARY SYSTEM																											
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																											
PITUITARY CARCINOMA,NOS ADENOMA, NOS ACIDOPHIL CARCINOMA	+ X	+	+ X	+	+	+	+	+ X	+	+	+	+	+	-	+	+	+	+ X	+	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID FOLLICULAR-CELL ADENOMA	+	+	+ X	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	-	+	+	-	-	+	-	-	-	+	+	-	+	-	+	-	+	-	+	-	+	+	+	+	-	+	+
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND ADENOMA, NOS ADENOCARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+ X	+	+	+
UTERUS ENDOMETRIAL STROMAL POLYP HEMANGIOSARCOMA	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																											
BRAIN ACIDOPHIL CARCINOMA, INVASIVE	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																											
HARDERIAN GLAND ADENOMA, NOS CYSTADENOMA, NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS MALIG.LYMPHOMA, LYMPHOCYTIC TYPE MALIG.LYMPHOMA, HISTIOCYTIC TYPE	M	M	M	M	M	M	M	M	M	M	M	M	M X	M	M	M	M	M	M	M	M	M	M X	M	M	M	M

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
M: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	0 2 6 7	0 2 7 8	0 2 8 9	0 3 0 1	0 3 1 2	0 3 1 3	0 3 1 4	0 3 1 5	0 3 1 6	0 3 1 7	0 3 1 8	0 3 1 9	0 4 0 1	0 4 0 2	0 4 0 3	0 4 0 4	0 4 0 5	0 4 0 6	0 4 0 7	0 4 0 8	0 4 0 9	0 4 1 0	0 4 1 1	0 4 1 2	0 4 1 3	0 4 1 4	0 4 1 5	0 4 1 6	0 4 1 7	0 4 1 8	0 4 1 9	0 4 2 0	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1 0 6	1 0 6	1 0 6	1 0 9	1 0 8	1 0 4	1 0 4	1 0 7	1 0 6	1 0 9	1 0 2	1 0 6	1 0 7	1 0 4	1 0 8	1 0 4	1 0 9	1 0 9	1 0 8	1 0 9	1 0 8	1 0 8	1 0 5	1 1 0	1 1 0	1 0 9	1 0 8	1 0 9	1 0 8	1 0 9	1 0 9	1 0 9	1 0 9	
INTEGUMENTARY SYSTEM																																	
SUBCUTANEOUS TISSUE HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M 1
RESPIRATORY SYSTEM																																	
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+	+	+	X	+	–	+	+	+	+	+	+	–	+	47 2
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																																	
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	–	+						44
CIRCULATORY SYSTEM																																	
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																																	
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER HEPATOCELLULAR ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	X	+	+	+	+	+	+	50 2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	H	+	H	H	+	H	+	+	H	+	+	+	+	H	+	+	+	+	+	+	+	+	+	+	+	+	50V
PANCREAS	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SMALL INTESTINE	+	+	+	+	+	–	+	+	–	–	+	+	+	–	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	48
LARGE INTESTINE	+	+	+	+	+	–	+	+	–	+	+	+	+	–	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	42
URINARY SYSTEM																																	
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																																	
PITUITARY CARCINOMA,NOS ADENOMA, NOS ACIDOPHIL CARCINOMA	+ X	+ X	+ X	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47 3 3 1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48 1
PARATHYROID	+	+	–	+	+	+	+	+	–	+	–	–	–	+	+	+	+	–	+	+	+	+	+	–	+	+	–						38
REPRODUCTIVE SYSTEM																																	
MAMMARY GLAND ADENOMA, NOS ADENOCARCINOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M 1 1
UTERUS ENDOMETRIAL STROMAL POLYP HEMANGIOSARCOMA	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50 2 1
OVARY	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+						49
NERVOUS SYSTEM																																	
BRAIN ACIDOPHIL CARCINOMA, INVASIVE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50 1
SPECIAL SENSE ORGANS																																	
HARDERIAN GLAND ADENOMA, NOS CYSTADENOMA, NOS	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N	N	N	50M 1 1
ALL OTHER SYSTEMS																																	
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS MALIG.LYMPHOMA, LYMPHOCYTIC TYPE MALIG.LYMPHOMA, HISTIOCYTIC TYPE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N	N X	N X	N	N	N	N	N	N	N	50M 1 1 1

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
–: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
H: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

LOW DOSE

ANIMAL NUMBER	0 1 1	0 1 2	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 2 1	0 2 2	0 2 3	0 2 4	0 2 5	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5
WEEKS ON STUDY	0 9 1	0 0 5	0 9 9	0 7 3	0 2 8	0 9 5	0 0 5	0 1 5	0 8 5	0 3 5	0 5 5	0 8 5	0 0 5	0 0 5	0 9 7	0 8 5	0 8 3	0 0 5	0 1 5	0 0 5	0 7 4	0 7 6	0 5 5	0 0 5	0 1 5	0 0 5
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	H	+	+	+	+	+	+	+	+	+
HEMANGIOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	H	+	+	+	+	+	+	+	+	+
MALIGNANT MELANOMA														X											
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
MALIGNANT LYMPHOMA, MIXED TYPE												X													
THYMUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
HEPATOCELLULAR ADENOMA																						X			
HEPATOCELLULAR CARCINOMA														X											
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	H	+	N	+
PANCREAS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
SQUAMOUS CELL PAPILLOMA																						X			
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
CARCINOMA,NOS	X	X						X						X					X						
ADENOMA, NOS																									X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+
FOLLICULAR-CELL ADENOMA								X						X											
PARATHYROID	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	-	+
PANCREATIC ISLETS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
ISLET-CELL ADENOMA																		X							
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	H	+	+	+	+	+	+	N	+	+
ADENOCARCINOMA, NOS		X																							
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
ADENOCARCINOMA, NOS																									
OVARY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	A	+	+
HEMANGIOSARCOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
BODY CAVITIES																									
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEMANGIOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																	X								
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50M
HEMANGIOMA	1
SUBCUTANEOUS TISSUE	50M
MALIGNANT MELANOMA	1
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	49
ALVEOLAR/BRONCHIOLAR ADENOMA	1
ALVEOLAR/BRONCHIOLAR CARCINOMA	2
TRACHEA	47
HEMATOPOIETIC SYSTEM	
BONE MARROW	49
SPLEEN	48
LYMPH NODES	47
MALIGNANT LYMPHOMA, MIXED TYPE	1
THYMUS	45
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	49
LIVER	49
HEPATOCELLULAR ADENOMA	1
HEPATOCELLULAR CARCINOMA	2
BILE DUCT	49
GALLBLADDER & COMMON BILE DUCT	38B
PANCREAS	49
ESOPHAGUS	50
STOMACH	47
SQUAMOUS CELL PAPILLOMA	1
SMALL INTESTINE	44
LARGE INTESTINE	43
URINARY SYSTEM	
KIDNEY	48
URINARY BLADDER	47
ENDOCRINE SYSTEM	
PITUITARY	45
CARCINOMA,NOS	3
ADENOMA, NOS	3
ADRENAL	47
THYROID	47
FOLLICULAR-CELL ADENOMA	3
PARATHYROID	46
PANCREATIC ISLETS	45
ISLET-CELL ADENOMA	1
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
ADENOCARCINOMA, NOS	1
UTERUS	47
ADENOCARCINOMA, NOS	1
OVARY	44
HEMANGIOSARCOMA	1
NERVOUS SYSTEM	
BRAIN	50
SPECIAL SENSE ORGANS	
HARDERIAN GLAND	50M
ADENOMA, NOS	1
BODY CAVITIES	
MESENTERY	50M
HEMANGIOMA	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
MALIGNANT LYMPHOMA, NOS	1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2

M ANIMALS NECROPSIED

\+ : TISSUE EXAMINED MICROSCOPICALLY
\- : REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X : TUMOR INCIDENCE
M : NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I : NO TISSUE INFORMATION SUBMITTED
C : NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A : AUTOLYSIS
M : ANIMAL MISSING
B : NO NECROPSY PERFORMED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE

ANIMAL NUMBER	0 0 1	0 0 2	0 0 3	0 0 4	0 0 5	0 0 6	0 0 7	0 0 8	0 0 9	0 1 0	0 1 1	0 1 2	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 2 1	0 2 2	0 2 3	0 2 4	0 2 5
WEEKS ON STUDY	0 4 6	0 9 5	1 0 4	0 9	0 7 6	0 9 5	0 8 7	1 0 8	0 7 8	1 0 5	0 0 2	0 9 6	0 0 1	0 3 9	0 9 5	0 9 3	0 9 5	1 0 7	0 7 8	1 0 4	1 0 4	1 0 2	1 0 4	1 0 7	1 0 4
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROUS HISTIOCYTOMA, MALIGNANT																	X								
LYMPHANGIOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																									
ALVEOLAR/BRONCHIOLAR CARCINOMA						X							X			X									
OSTEOSARCOMA, METASTATIC																			X						
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																						X			
MALIGNANT LYMPHOMA, MIXED TYPE																						X			
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA																									
KUPFFER-CELL SARCOMA																									
UNDIFFERENTIATED LEUKEMIA																						X			
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	N	+	+	H	+	+	H	+	+	+	+	+	N	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS														X	X										X
ADRENAL	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA										X															
FOLLICULAR-CELL CARCINOMA													X												
PARATHYROID	-	-	+	+	-	-	-	+	+	+	-	+	+	-	-	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	H	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS															X										
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
OVARY	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TERATOMA, NOS														X											
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
BONE	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
OSTEOSARCOMA																			X						
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H	H
FIBROUS HISTIOCYTOMA, MALIGNANT															X			X							
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
LYMPHOCYTIC LEUKEMIA						X																			

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
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H: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	0 2 4 1	0 2 7 1	0 2 8 1	0 2 9 1	0 3 1 1	0 3 2 1	0 3 3 1	0 3 5 1	0 3 5 1	0 3 6 1	0 3 7 1	0 3 8 1	0 3 9 1	0 4 0 1	0 4 1 1	0 4 2 1	0 4 3 1	0 4 4 1	0 4 5 1	0 4 6 1	0 4 7 1	0 4 8 1	0 4 9 1	0 5 0 1	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1 9 1	5 1 4	6 0 1	8 5 1	0 7 3	0 1 3	1 1 7	1 0 4	1 0 4	1 0 4	0 7 1	0 4 0	0 5 2	1 0 4	1 0 6	1 0 4	1 0 4	1 0 4	1 0 7	1 0 5	1 0 4	1 0 8	1 0 9	1 0 5	
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
FIBROUS HISTIOCYTOMA, MALIGNANT														X											1
LYMPHANGIOMA																									1
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
SQUAMOUS CELL CARCINOMA, METASTAT																						X			1
ALVEOLAR/BRONCHIOLAR CARCINOMA																									3
OSTEOSARCOMA, METASTATIC																									1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
HEMANGIOSARCOMA																									1
MALIGNANT LYMPHOMA, MIXED TYPE																									1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	-	+	-	+	+	+	+	44
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR CARCINOMA					X																				3
KUPFFER-CELL SARCOMA																				X					1
UNDIFFERENTIATED LEUKEMIA																									1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	N	+	+	+	N	A	+	+	+	+	+	+	+	+	+	N	+	44
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	A	+	-	-	+	+	+	-	+	+	-	-	44
ADENOMA, NOS														X											4
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	47
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	47
FOLLICULAR-CELL ADENOMA																	X								1
FOLLICULAR-CELL CARCINOMA																									2
PARATHYROID	+	+	-	+	+	+	-	-	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	+	37
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
ADENOCARCINOMA, NOS																									1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
SQUAMOUS CELL CARCINOMA																						X			1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	48
TERATOMA, NOS																									1
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	49
MUSCULOSKELETAL SYSTEM																									
BONE	M	M	M	M	M	M	M	M	M	M	M	M	A	M	M	M	M	M	M	M	M	M	M	M	49
OSTEOSARCOMA																									1
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	A	M	M	M	M	M	M	M	M	M	M	M	49
FIBROUS HISTIOCYTOMA, MALIGNANT										X								X							1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									2
LYMPHOCYTIC LEUKEMIA																									1

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
#SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	3 (6%)	1 (2%)	3 (6%)
#SUBCUT TISSUE	(50)	(50)	(50)
HEMATOMA, NOS		1 (2%)	
GRANULOMA, FOREIGN BODY	1 (2%)		
FIBROSIS	1 (2%)		
RESPIRATORY SYSTEM			
@LUNG	(49)	(49)	(48)
EDEMA, NOS	1 (2%)		
PNEUMONIA, ASPIRATION	1 (2%)		4 (8%)
INFLAMMATION, SUPPURATIVE	2 (4%)		
BRONCHOPNEUMONIA, CHRONIC			1 (2%)
CHOLESTEROL DEPOSIT			1 (2%)
HYPERPLASIA, ADENOMATOUS			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM		3 (6%)	1 (2%)
METAPLASIA, OSSEOUS			1 (2%)
HEMATOPOIETIC SYSTEM			
@BONE MARROW	(48)	(49)	(50)
HYPERPLASIA, NOS	2 (4%)		
MYELOFIBROSIS	1 (2%)		
@SPLEEN	(50)	(49)	(50)
CONGESTION, NOS	2 (4%)		
FIBROSIS, MULTIFOCAL	1 (2%)		
METAMORPHOSIS FATTY	1 (2%)		
HEMOSIDEROSIS	20 (40%)	20 (41%)	7 (14%)

@ NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
# NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANGIECTASIS	1 (2%)		
HYPERPLASIA, LYMPHOID	2 (4%)		
HEMATOPOIESIS	1 (2%)	2 (4%)	
#LYMPH NODE	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)		
#MANDIBULAR L. NODE	(50)	(50)	(50)
HYPERPLASIA, PLASMA CELL		1 (2%)	
#MESENTERIC L. NODE	(50)	(50)	(50)
HEMORRHAGE, CHRONIC			
INFLAMMATION, GRANULOMATOUS			
ANGIECTASIS	1 (2%)		
#INGUINAL LYMPH NODE	(50)	(50)	(50)
HYPERPLASIA, DIFFUSE			
#PANCREAS	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(50)
MINERALIZATION	1 (2%)		
INFLAMMATION, CHRONIC			
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	1 (2%)
FIBROSIS, FOCAL	23 (46%)	23 (46%)	19 (38%)
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC		2 (4%)	5 (10%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
*DESCENDING THORACIC	(50)	(50)	(50)
ARTERIOSCLEROSIS, NOS	1 (2%)		
*MESENTERIC ARTERY	(50)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
#PANCREAS	(50)	(50)	(49)
PERIARTERITIS			
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(50)	(50)
FIBROSIS, FOCAL		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ATROPHY, FOCAL		1 (2%)	
#LIVER	(50)	(50)	(50)
CONGESTION, ACUTE			1 (2%)
INFLAMMATION, GRANULOMATOUS			1 (2%)
NECROSIS, ZONAL	1 (2%)		
CYTOPLASMIC VACUOLIZATION	2 (4%)		
CYTOLOGIC ALTERATION, NOS	3 (6%)	4 (8%)	1 (2%)
ANGIECTASIS			2 (4%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION		1 (2%)	
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	11 (22%)	32 (64%)	10 (20%)
HYPERPLASIA, FOCAL	14 (28%)	1 (2%)	1 (2%)
#PANCREAS	(50)	(50)	(49)
CYST, NOS			1 (2%)
ATROPHY, FOCAL	4 (8%)	5 (10%)	1 (2%)
#PANCREATIC ACINUS	(50)	(50)	(49)
ATROPHY, NOS	1 (2%)		
#GASTRIC SUBMUCOSA	(49)	(50)	(49)
FIBROSIS		1 (2%)	
#COLON	(48)	(49)	(49)
PARASITISM		1 (2%)	1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
INFLAMMATION, CHRONIC	40 (80%)	23 (46%)	20 (40%)
NEPHROSIS, NOS		1 (2%)	1 (2%)
PIGMENTATION, NOS		1 (2%)	
#KIDNEY/TUBULE	(50)	(50)	(50)
DEGENERATION, HYALINE	1 (2%)		
#URINARY BLADDER	(49)	(49)	(49)
INFLAMMATION, HEMORRHAGIC			1 (2%)
HYPERPLASIA, NODULAR			6 (12%)
HYPERPLASIA, EPITHELIAL		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(49)	(49)
ANGIECTASIS		1 (2%)	1 (2%)
#ADRENAL	(50)	(50)	(50)
CYST, NOS		1 (2%)	
CYTOPLASMIC VACUOLIZATION		1 (2%)	
#ADRENAL CORTEX	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION		2 (4%)	
ANGIECTASIS	1 (2%)		
#ADRENAL MEDULLA	(50)	(50)	(50)
NECROSIS, NOS		1 (2%)	
HYPERPLASIA, FOCAL	2 (4%)		
#THYROID	(48)	(50)	(50)
CYSTIC FOLLICLES	7 (15%)	1 (2%)	1 (2%)
HYPERPLASIA, C-CELL		3 (6%)	
#PARATHYROID	(42)	(50)	(45)
HYPERPLASIA, NOS			
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
CYSTIC DUCTS	13 (26%)	15 (30%)	6 (12%)
HYPERPLASIA, NOS			1 (2%)
ADENOSIS	3 (6%)		
*PENIS	(50)	(50)	(50)
PROLAPSE	1 (2%)		
*PREPUTIAL GLAND	(50)	(50)	(50)
CYST, NOS		1 (2%)	2 (4%)
CYSTIC DUCTS	6 (12%)	3 (6%)	1 (2%)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION, ACUTE SUPPURATIVE			1 (2%)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC SUPPURATIV			
HYPERPLASIA, NOS			
HYPERPLASIA, CYSTIC			

NUMBER OF AHIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PROSTATE	(49)	(49)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE	10 (20%)	4 (8%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL			
#PROSTATIC GLAND	(49)	(49)	(49)
ABSCESS, CHRONIC		1 (2%)	
*SEMINAL VESICLE	(50)	(50)	(50)
DILATATION, NOS		1 (2%)	1 (2%)
CYST, NOS			
INFLAMMATION, ACUTE FOCAL			
GRANULOMA, SPERMATIC			
#TESTIS	(50)	(50)	(49)
ATROPHY, NOS		1 (2%)	
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(49)	(50)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
#HYPOTHALAMUS	(50)	(49)	(50)
HEMORRHAGE			
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
RETINOPATHY	9 (18%)	6 (12%)	39 (78%)
CATARACT	7 (14%)	6 (12%)	13 (26%)
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)		
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NECROSIS, FAT	14 (28%)	9 (18%)	8 (16%)
ANGIECTASIS			1 (2%)
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NONE			

@ NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
#SKIN	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, ACUTE FOCAL		1 (2%)	
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC			
#SUBCUT TISSUE	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST			1 (2%)
CONGESTION, NOS		1 (2%)	
HEMORRHAGE		2 (4%)	
PROTEINOSIS, ALVEOLAR		1 (2%)	
CHOLESTEROL DEPOSIT	1 (2%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM			
HEMATOPOIETIC SYSTEM			
#SPLEEN	(50)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
FIBROSIS, FOCAL	1 (2%)		
HEMOSIDEROSIS	30 (60%)	30 (60%)	27 (54%)
ANGIECTASIS			1 (2%)
HEMATOPOIESIS	1 (2%)	1 (2%)	
#MEDIASTINAL L.NODE	(50)	(50)	(50)
HEMOSIDEROSIS	1 (2%)		

@ NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
# NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PANCREATIC L.NODE	(50)	(50)	(50)
ANGIECTASIS			
#PEYER'S PATCH	(49)	(48)	(48)
HYPERPLASIA, LYMPHOID			1 (2%)
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	1 (2%)
FIBROSIS, FOCAL	10 (20%)	8 (16%)	8 (16%)
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC		2 (4%)	
*MESENTERIC ARTERY	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS		1 (2%)	
#KIDNEY/GLOMERULUS	(50)	(50)	(50)
EMBOLISM, NOS		1 (2%)	
#ADRENAL	(50)	(50)	(50)
EMBOLISM, NOS		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
NECROSIS, FOCAL		1 (2%)	
NECROSIS, ZONAL		1 (2%)	
CYTOPLASMIC VACUOLIZATION			
CYTOLOGIC ALTERATION, NOS	3 (6%)	2 (4%)	3 (6%)
HYPERPLASIA, NOS			1 (2%)
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	8 (16%)	21 (42%)	23 (46%)
HYPERPLASIA, FOCAL	12 (24%)	4 (8%)	1 (2%)
#PANCREAS	(49)	(49)	(50)
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
FIBROSIS, FOCAL	1 (2%)		
ATROPHY, NOS		1 (2%)	1 (2%)
ATROPHY, FOCAL	3 (6%)	3 (6%)	1 (2%)
@COLON	(49)	(47)	(49)
PARASITISM	1 (2%)		1 (2%)
URINARY SYSTEM			
@KIDNEY	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)	2 (4%)	
FIBROSIS, FOCAL	1 (2%)	1 (2%)	
NEPHROSIS, NOS			1 (2%)
PIGMENTATION, NOS		1 (2%)	
@URINARY BLADDER	(49)	(49)	(50)
HYPERPLASIA, EPITHELIAL			1 (2%)
ENDOCRINE SYSTEM			
@PITUITARY	(49)	(50)	(50)
CYST, NOS	1 (2%)		
HEMOSIDEROSIS	1 (2%)		
ANGIECTASIS	2 (4%)	3 (6%)	1 (2%)
@ADRENAL	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION			2 (4%)
ANGIECTASIS		1 (2%)	
@ADRENAL CORTEX	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION	5 (10%)	6 (12%)	3 (6%)
ANGIECTASIS			1 (2%)
@THYROID	(50)	(48)	(50)
ULTIMOBRANCHIAL CYST			1 (2%)
CYSTIC FOLLICLES	2 (4%)	1 (2%)	
FOLLICULAR CYST, NOS			
ATROPHY, CYSTIC		1 (2%)	
HYPERPLASIA, EPITHELIAL			1 (2%)
HYPERPLASIA, C-CELL		1 (2%)	1 (2%)
REPRODUCTIVE SYSTEM			
#MAMMARY GLAND	(50)	(50)	(50)
CYSTIC DUCTS	30 (60%)	30 (60%)	36 (72%)

@ NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
# NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NOS			3 (6%)
HYPERPLASIA, CYSTIC			5 (10%)
ADENOSIS	5 (10%)	9 (18%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
CYSTIC DUCTS	1 (2%)	6 (12%)	2 (4%)
INFLAMMATION, ACUTE SUPPURATIVE		3 (6%)	1 (2%)
HYPERPLASIA, NOS	1 (2%)	1 (2%)	1 (2%)
*CLITORAL GLAND	(50)	(50)	(50)
CYST, NOS		1 (2%)	
CYSTIC DUCTS		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE			1 (2%)
#UTERUS	(50)	(49)	(50)
HEMATOMETRA	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, EPITHELIAL			
ANGIECTASIS			1 (2%)
#UTERUS/ENDOMETRIUM	(50)	(49)	(50)
EDEMA, NOS		1 (2%)	
HEMATOMETRA		2 (4%)	
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE			
HYPERPLASIA, NOS	1 (2%)		3 (6%)
HYPERPLASIA, CYSTIC	9 (18%)	5 (10%)	2 (4%)
#ENDOMETRIAL GLAND	(50)	(49)	(50)
HYPERPLASIA, CYSTIC		1 (2%)	
#OVARY	(50)	(50)	(50)
CYST, NOS	3 (6%)		1 (2%)
FOLLICULAR CYST, NOS		1 (2%)	
NERVOUS SYSTEM			
#CEREBRAL VENTRICLE	(50)	(50)	(50)
HYDROCEPHALUS, NOS			1 (2%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
RETINOPATHY	4 (8%)	35 (70%)	11 (22%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CATARACT	2 (4%)	33 (66%)	9 (18%)
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS		1 (2%)	
*EYELID	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*STERNUM	(50)	(50)	(50)
CYST, NOS			
BODY CAVITIES			
*MEDIASTINAL PLEURA	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
*MESENTERY	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
HEMORRHAGE			
FIBROSIS, FOCAL		1 (2%)	
NECROSIS, FAT	8 (16%)	18 (36%)	13 (26%)
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	3	1	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
ULCER, FOCAL			1 (2%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC			2 (4%)
FIBROSIS			1 (2%)
FIBROSIS, FOCAL	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV			2 (4%)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS	1 (2%)		
NECROSIS, FOCAL			3 (6%)
NECROSIS, FAT		1 (2%)	
FOREIGN MATERIAL, NOS			
RESPIRATORY SYSTEM			
#LUNG/BRONCHIOLE	(50)	(50)	(50)
HYPERPLASIA, NOS	2 (4%)		1 (2%)
#LUNG	(50)	(50)	(50)
EDEMA, NOS			1 (2%)
HEMORRHAGE	2 (4%)		
BRONCHOPNEUMONIA, FOCAL	2 (4%)		
LYMPHOCYTIC INFLAMMATORY INFILTR			
INFLAMMATION, INTERSTITIAL	1 (2%)		1 (2%)
BRONCHOPNEUMONIA SUPPURATIVE		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
PNEUMONIA, CHRONIC MURINE	3 (6%)		1 (2%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
INFLAMMATION, GRANULOMATOUS	1 (2%)	2 (4%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, FOCAL GRANULOMATOU	3 (6%)		
REACTION, FOREIGN BODY	1 (2%)		
CHOLESTEROL DEPOSIT		2 (4%)	
HYPERPLASIA, ADENOMATOUS	8 (16%)	12 (24%)	15 (30%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	3 (6%)	1 (2%)	2 (4%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
HYPERPLASIA, HEMATOPOIETIC	1 (2%)		
HYPERPLASIA, LYMPHOID	1 (2%)		
#SPLEEN	(49)	(48)	(50)
ANGIECTASIS		1 (2%)	
HYPERPLASIA, LYMPHOID	1 (2%)		
HEMATOPOIESIS	2 (4%)		1 (2%)
#MANDIBULAR L. NODE	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)
#MESENTERIC L. NODE	(50)	(49)	(49)
HEMORRHAGE	2 (4%)		
ANGIECTASIS	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	2 (4%)
HEMATOPOIESIS			
#INGUINAL LYMPH NODE	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID	2 (4%)		1 (2%)
#LUNG/BRONCHUS	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID			
#PEYER'S PATCH	(45)	(42)	(45)
HYPERPLASIA, LYMPHOID	5 (11%)	4 (10%)	2 (4%)
#THYMUS	(41)	(48)	(46)
CYST, NOS	1 (2%)		
ATROPHY, NOS			1 (2%)
HYPERPLASIA, LYMPHOID		1 (2%)	
CIRCULATORY SYSTEM			
#ILIAC LYMPH NODE	(50)	(49)	(49)
LYMPHANGIECTASIS			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#AURICULAR APPENDAGE	(50)	(50)	(50)
PERIARTERITIS			
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, NECROTIZING			1 (2%)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
INFLAMMATION, CHRONIC FOCAL	2 (4%)		
*BLOOD VESSEL	(50)	(50)	(50)
DEGENERATION PIGMENTARY	1 (2%)		
*AORTA	(50)	(50)	(50)
CALCIFICATION, FOCAL	1 (2%)		
#LIVER	(49)	(49)	(50)
THROMBOSIS, NOS	1 (2%)		
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS			1 (2%)
#KIDNEY	(49)	(49)	(50)
PERIARTERITIS	1 (2%)		1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(49)	(50)
HEMORRHAGE	1 (2%)		
INFLAMMATION, GRANULOMATOUS	1 (2%)		
FIBROSIS, FOCAL			1 (2%)
CHOLESTEROL DEPOSIT	1 (2%)		
#LIVER	(49)	(49)	(50)
INFLAMMATION, ACUTE FIBRINOUS	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		
NECROSIS, NOS			1 (2%)
NECROSIS, COAGULATIVE	1 (2%)	1 (2%)	1 (2%)
CYTOPLASMIC CHANGE, NOS			
CYTOPLASMIC VACUOLIZATION		4 (8%)	10 (20%)
FOCAL CELLULAR CHANGE	2 (4%)	1 (2%)	2 (4%)
HYPERPLASIA, FOCAL	1 (2%)		
#LIVER/CENTRILOBULAR	(49)	(49)	(50)
CYTOPLASMIC VACUOLIZATION	2 (4%)	4 (8%)	3 (6%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*GALLBLADDER	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)		
@BILE DUCT	(49)	(49)	(50)
CYST, NOS		1 (2%)	
@ESOPHAGUS	(50)	(50)	(49)
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, GRANULOMATOUS	3 (6%)	1 (2%)	1 (2%)
@GASTRIC MUCOSA	(49)	(48)	(48)
EPIDERMAL INCLUSION CYST	1 (2%)		
@ILEUM	(45)	(42)	(45)
DIVERTICULUM		1 (2%)	
URINARY SYSTEM			
@KIDNEY	(49)	(49)	(50)
PYELONEPHRITIS, FOCAL	1 (2%)		
INFLAMMATION, INTERSTITIAL	1 (2%)		2 (4%)
PYELONEPHRITIS, ACUTE/CHRONIC			
NEPHROPATHY	3 (6%)		
DEGENERATION PIGMENTARY	1 (2%)		
NEPHROSIS, NOS		1 (2%)	
METAPLASIA, OSSEOUS			1 (2%)
@KIDNEY/PELVIS	(49)	(49)	(50)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
ENDOCRINE SYSTEM			
@PITUITARY	(46)	(46)	(46)
CYST, NOS	1 (2%)		
@ADRENAL	(47)	(49)	(50)
CYTOLOGIC ALTERATION, NOS			
@ADRENAL MEDULLA	(47)	(49)	(50)
HYPERPLASIA, NOS			1 (2%)
@THYROID	(50)	(45)	(50)
CYSTIC FOLLICLES		1 (2%)	1 (2%)

@ NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOLLICULAR CYST, NOS	2 (4%)		
INFLAMMATION, SUPPURATIVE	1 (2%)		
REACTION, FOREIGN BODY	1 (2%)		
DEGENERATION, CYSTIC	1 (2%)		
HYPERPLASIA, FOLLICULAR-CELL			1 (2%)
#THYROID FOLLICLE	(50)	(45)	(50)
HYPERPLASIA, CYSTIC	1 (2%)		
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST		1 (2%)	
CYSTIC DUCTS	2 (4%)	2 (4%)	6 (12%)
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, NOS		1 (2%)	
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)	1 (2%)	1 (2%)
#PROSTATE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
HYPERPLASIA, EPITHELIAL			1 (2%)
#TESTIS	(50)	(50)	(50)
NECROSIS, FOCAL	1 (2%)		
ATROPHY, NOS	1 (2%)		
HYPERPLASIA, INTERSTITIAL CELL		1 (2%)	
*EPIDIDYMIS	(50)	(50)	(50)
ULCER, NOS		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
CORPORA AMYLACEA		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
ATROPHY, NOS	1 (2%)		
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
#INTERCOSTAL MUSCLE	(50)	(50)	(50)
INFLAMMATION, NECROTIZING		1 (2%)	
BODY CAVITIES			
#MEDIASTINUM	(50)	(50)	(50)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	1 (2%)	
#PERICARDIUM	(50)	(50)	(50)
EDEMA, NOS		1 (2%)	
REACTION, FOREIGN BODY		1 (2%)	
NECROSIS, FAT		1 (2%)	
#MESENTERY	(50)	(50)	(50)
HEMORRHAGIC CYST	1 (2%)		
STEATITIS	2 (4%)		2 (4%)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
NECROSIS, FAT	2 (4%)	1 (2%)	3 (6%)
ALL OTHER SYSTEMS			
#MULTIPLE ORGANS	(50)	(50)	(50)
ULCER, FOCAL			1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
OMENTUM			
STEATITIS	1		
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED		10	5
AUTO/NECROPSY/NO HISTO			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(49)
EPIDERMAL INCLUSION CYST			1 (2%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(49)
ABSCESS, NOS		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
REACTION, FOREIGN BODY		1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS		1 (2%)	
CHOLESTEROL DEPOSIT		1 (2%)	1 (2%)
RESPIRATORY SYSTEM			
#TRACHEA	(47)	(47)	(48)
PENETRATING WOUND		1 (2%)	
#LUNG/BRONCHIOLE	(47)	(49)	(49)
HYPERPLASIA, NOS		1 (2%)	
#LUNG	(47)	(49)	(49)
HEMORRHAGE		1 (2%)	1 (2%)
INFLAMMATION, INTERSTITIAL			2 (4%)
PNEUMONIA, ASPIRATION		1 (2%)	
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
BRONCHOPNEUMONIA SUPPURATIVE			1 (2%)
PNEUMONIA, CHRONIC MURINE	4 (9%)		2 (4%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU			2 (4%)
CHOLESTEROL DEPOSIT		1 (2%)	1 (2%)
HYPERPLASIA, ADENOMATOUS	3 (6%)	2 (4%)	3 (6%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)	2 (4%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
*MULTIPLE ORGANS	(50)	(50)	(49)
HYPERPLASIA, HEMATOPOIETIC	3 (6%)		
HYPERPLASIA, LYMPHOID	2 (4%)		1 (2%)
HEMATOPOIESIS		1 (2%)	
#BONE MARROW	(49)	(49)	(49)
HYPERPLASIA, NOS	2 (4%)	2 (4%)	1 (2%)
MYELOFIBROSIS		4 (8%)	
HYPERPLASIA, HEMATOPOIETIC		2 (4%)	1 (2%)
HYPERPLASIA, GRANULOCYTIC		1 (2%)	4 (8%)
HYPERPLASIA, RETICULUM CELL	1 (2%)		
#SPLEEN	(47)	(48)	(49)
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, HEMATOPOIETIC			1 (2%)
HYPERPLASIA, LYMPHOID	2 (4%)	4 (8%)	2 (4%)
HEMATOPOIESIS	3 (6%)	10 (21%)	5 (10%)
MYELOPOIESIS			
#SPLENIC CAPSULE	(47)	(48)	(49)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#LYMPH NODE	(50)	(47)	(49)
HYPERPLASIA, NOS	1 (2%)		
#MANDIBULAR L. NODE	(50)	(47)	(49)
HYPERPLASIA, LYMPHOID		1 (2%)	
#CERVICAL LYMPH NODE	(50)	(47)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)
#PANCREATIC L.NODE	(50)	(47)	(49)
HYPERPLASIA, NOS			1 (2%)
#MESENTERIC L. NODE	(50)	(47)	(49)
HEMORRHAGIC CYST		1 (2%)	
INFLAMMATION, GRANULOMATOUS		1 (2%)	
#RENAL LYMPH NODE	(50)	(47)	(49)
HYPERPLASIA, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, LYMPHOID		3 (6%)	
#ILIAC LYMPH NODE	(50)	(47)	(49)
ANGIECTASIS			
#LUNG/BRONCHUS	(47)	(49)	(49)
HYPERPLASIA, LYMPHOID			
#LUNG	(47)	(49)	(49)
HYPERPLASIA, LYMPHOID		1 (2%)	1 (2%)
#LIVER	(50)	(49)	(49)
LEUKOCYTOSIS, NOS	1 (2%)		
HEMATOPOIESIS	1 (2%)	4 (8%)	1 (2%)
MYELOPOIESIS			
#PEYER'S PATCH	(40)	(44)	(47)
HYPERPLASIA, LYMPHOID	1 (3%)		
#KIDNEY	(50)	(48)	(49)
PLASMACYTOSIS		1 (2%)	
HYPERPLASIA, LYMPHOID			1 (2%)
#THYMUS	(44)	(45)	(44)
INFLAMMATION, CHRONIC		1 (2%)	
ATROPHY, NOS			1 (2%)
HYPERPLASIA, LYMPHOID		1 (2%)	
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(49)
PERIARTERITIS		1 (2%)	
#ENDOCARDIUM	(49)	(50)	(49)
FIBROSIS, FOCAL			1 (2%)
*AORTA	(50)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
*CORONARY ARTERY	(50)	(50)	(49)
INFLAMMATION, NECROTIZING			1 (2%)
HYPERTROPHY, FOCAL			1 (2%)
#PANCREAS	(47)	(45)	(49)
PERIARTERITIS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#OVARY	(49)	(44)	(48)
THROMBOSIS, NOS		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEMORRHAGIC CYST	1 (2%)		
INFLAMMATION, NOS			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	3 (6%)	2 (4%)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
NECROSIS, FOCAL	1 (2%)		
NUCLEAR ENLARGEMENT	1 (2%)		
INCLUSION, NUCLEAR	1 (2%)		
CYTOPLASMIC CHANGE, NOS		1 (2%)	1 (2%)
CYTOPLASMIC VACUOLIZATION		1 (2%)	1 (2%)
FOCAL CELLULAR CHANGE			
HYPERPLASIA, FOCAL	1 (2%)		
*GALLBLADDER	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#PANCREAS	(47)	(45)	(49)
CYSTIC DUCTS		2 (4%)	
EDEMA, NOS			1 (2%)
INFLAMMATION, INTERSTITIAL		1 (2%)	
INFLAMMATION, SUPPURATIVE		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		
NECROSIS, FAT		1 (2%)	
ATROPHY, NOS			1 (2%)
*OROPHARYNX	(50)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
#ESOPHAGUS	(49)	(50)	(49)
PENETRATING WOUND		1 (2%)	
INFLAMMATION ACUTE AND CHRONIC			1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	
INFLAMMATION, GRANULOMATOUS	5 (10%)		
#CARDIAC STOMACH	(47)	(47)	(49)
ULCER, NOS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, BASAL CELL	1 (2%)		
#INTESTINAL VILLUS	(40)	(44)	(47)
CYTOPLASMIC VACUOLIZATION			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(48)	(49)
HYDRONEPHROSIS			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
INFLAMMATION, INTERSTITIAL		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)		
NEPHROPATHY	1 (2%)		1 (2%)
NECROSIS, MEDULLARY		1 (2%)	
HYPOPLASIA, NOS			1 (2%)
#KIDNEY/PELVIS	(50)	(48)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR			
INFLAMMATION, NECROTIZING	1 (2%)	1 (2%)	
#URINARY BLADDER	(47)	(47)	(47)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(45)	(44)
HYPERPLASIA, NOS	3 (6%)		
HYPERPLASIA, FOCAL			3 (7%)
ANGIECTASIS	1 (2%)	2 (4%)	
#THYROID	(48)	(47)	(47)
CYSTIC FOLLICLES	1 (2%)		1 (2%)
FOLLICULAR CYST, NOS			2 (4%)
DEGENERATION, CYSTIC	2 (4%)		
HYPERPLASIA, FOLLICULAR-CELL	1 (2%)		
#THYROID FOLLICLE	(48)	(47)	(47)
MULTIPLE CYSTS		1 (2%)	
HYPERPLASIA, PAPILLARY			1 (2%)
HYPERPLASIA, CYSTIC	1 (2%)		1 (2%)
REPRODUCTIVE SYSTEM			
#MAMMARY GLAND	(50)	(50)	(49)
CYSTIC DUCTS	4 (8%)	3 (6%)	2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FIBROSIS	1 (2%)		
HYPERPLASIA, NOS		2 (4%)	
*MAMMARY LOBULE	(50)	(50)	(49)
HYPERPLASIA, NOS	1 (2%)		
#UTERUS	(50)	(47)	(49)
HYDROMETRA		1 (2%)	
CYST, NOS	1 (2%)		1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
PYOMETRA	2 (4%)	1 (2%)	1 (2%)
ENDOMETRIAL POLYP		1 (2%)	
ANGIECTASIS	1 (2%)		
#UTERUS/ENDOMETRIUM	(50)	(47)	(49)
CYST, NOS	5 (10%)	3 (6%)	4 (8%)
INFLAMMATION, SUPPURATIVE	1 (2%)	3 (6%)	3 (6%)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, CYSTIC	5 (10%)	2 (4%)	8 (16%)
HYPERPLASIA, ADENOMATOUS			1 (2%)
ANGIECTASIS			
#ENDOMETRIAL GLAND	(50)	(47)	(49)
HYPERPLASIA, CYSTIC	18 (36%)	25 (53%)	14 (29%)
#OVARY	(49)	(44)	(48)
CYST, NOS	2 (4%)	1 (2%)	3 (6%)
CYSTIC FOLLICLES	1 (2%)		
FOLLICULAR CYST, NOS		1 (2%)	
HEMATOMA, NOS	1 (2%)		
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, CHRONIC	4 (8%)	2 (5%)	3 (6%)
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	1 (2%)		
#BRAIN	(50)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
CORPORA AMYLACEA			
#BRAIN/THALAMUS	(50)	(50)	(49)
PSAMMOMA BODIES	1 (2%)		1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(49)
PHTHISIS BULBI		1 (2%)	
*MIDDLE EAR	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	2 (4%)	1 (2%)	
INFLAMMATION, CHRONIC SUPPURATIV			1 (2%)
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(49)
FIBROUS DYSPLASIA	1 (2%)		
*CORTEX OF BONE	(50)	(50)	(49)
FIBROUS OSTEODYSTROPHY			3 (6%)
HYPERPLASIA, NOS		1 (2%)	
BODY CAVITIES			
*THORACIC CAVITY	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
REACTION, FOREION BODY			1 (2%)
*MEDIASTINUM	(50)	(50)	(49)
INFLAMMATION, GRANULOMATOUS	2 (4%)		1 (2%)
*PERITONEUM	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
INFLAMMATION, FIBRINOUS	1 (2%)		
INFLAMMATION, ACUTE SUPPURATIVE	2 (4%)		
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		2 (4%)
ABSCESS, CHRONIC	1 (2%)		
NECROSIS, FAT			1 (2%)
*PLEURA	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
*MEDIASTINAL PLEURA	(50)	(50)	(49)
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
REACTION, FOREIGN BODY		1 (2%)	
*MESENTERY	(50)	(50)	(49)
STEATITIS		1 (2%)	1 (2%)
INFLAMMATION, NECROTIZING	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC SUPPURATIV	2 (4%)		
NECROSIS, FAT	1 (2%)	3 (6%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR	9 (18%)	5 (10%)	4 (8%)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, ACUTE FIBRINOUS			
HYPERPLASIA, NOS			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	3	3	2
AUTO/NECROPSY/HISTO PERF		1	
AUTOLYSIS/NO NECROPSY			1

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX E

ANALYSIS OF ALLYL ISOTHIOCYANATE
LOT NO. 532251
(MIDWEST RESEARCH INSTITUTE)

APPENDIX E

A. ELEMENTAL ANALYSIS

Element	C	H	N	S
Theory	48.45	5.08	14.13	32.34
Determined	48.52	5.08	14.10	32.13
	48.56	5.13	14.18	32.27

B. BOILING POINT

Determined

151°C at 746.3 mm (visual, micro boiling point tube) 148° to 152°C (Dupont 900DTA)

Literature Values

152.05°C at 760 mm (Timmermans and Hennault-Roland, 1922)

C. DENSITY

Determined

d_{22}^{23}:1.016

Literature Value

d_4^{30}:1.00811 (variation 0.000103/°C) (Timmermans and Hennault-Roland, 1922)

D. REFRACTIVE INDEX

Determined

n_D^{20} 1.5315 ± 0.0002 (δ)

Literature Value

n_D^{17} 1.5336 (Timmermans and Hennault-Roland, 1922)

E. THIN-LAYER CHROMATOGRAPHY

Plates: Silica Gel 60 F254
Amount spotted: 100 and 300 μg

System 1: 95% Ethanol
R_f: 0.86
R_{st}: 1.13

System 2: Chloroform:1,4-Dioxane (95:5)
R_f: 0.55
R_{st}: 0.61

Ref. Standard: 1,1,3,3-Tetramethylthiourea
Visualization: Ultraviolet (254 nm), and I_2 vapor

APPENDIX E

F. VAPOR-PHASE CHROMATOGRAPHY

1. System 1

Instrument: Bendix 2500
Detector: Flame ionization
Column: Chromosorb 102, 1.8 m x 4 mm I.D.
Inlet temperature: 225°C
Detector temperature: 270°C
Oven temperature program: 2 min. at 150°C, then 150° to 200°C at 10°/min.
Results: Major peak and four impurities

Peak	Retention Time (min.)	Retention Time (Relative to Allyl Isothiocyanate)	Area (Relative to Allyl Isothiocyanate)
1	3.5	0.21	0.007
2	8.6	0.52	0.04
3	9.3	0.56	0.07
4	16.6	1.00	100
5	20.3	1.22	0.2

2. System 2

Instrument: Bendix 2500
Detector: Flame ionization
Column: 10% Carbowax 20 M, on 80/100 Chromosorb W (AW), 1.8 m x 4 mm I.D.
Inlet temperature: 225°C
Detector temperature: 270°C
Oven temperature program: 5 min. at 50°C, then 50° to 125°C at 10°C/min.
Results: Major peak and six impurities

Peak	Retention Time (min.)	Retention Time (Relative to Allyl Isothiocyanate)	Area (Relative to Allyl Isothiocyanate)
1	1.0	0.07	0.006
2	4.9	0.36	0.3
3	10.6	0.78	0.08
4	12.8	0.95	Shoulder 0.1%
5	13.5	1.00	100
6	15.2	1.13	0.5
7	16.0	1.19	0.04

G. SPECTRAL DATA

1. Infrared

Instrument: Beckman IR-12
Cell: Neat, sodium chloride plates
Results: See Figure 5

Consistent with literature spectrum (Sadtler Research Laboratories)

2. Ultraviolet/Visible

Instrument: Cary 118

Determined literature values (Sadtler Research Laboratories)

λ max (nm)	$\varepsilon \times 10^{-2}$	λ max (nm)	$\varepsilon \times 10^{-2}$
249	10.40 ± 0.01 (δ)	247	8.30

No absorbance between 350 and 800 nm (visible range) at a concentration of 1 mg/ml
Solvent: Hexane

(Calculated from graph of spectrum)

3. Nuclear Magnetic Resonance

Solvent: Dioxane

Instrument: Varian HA-100
Solvent: Chloroform-d with internal tetramethylsilane
Assignments (See Figure 6)

Identical to literature spectrum (Sadtler Research Laboratories)

(a) } d^2 δ 4.17 ppm
(b) } d
(c) m, δ 5.31 ppm
(d) m, δ 5.42 ppm
(e) t^4, δ 5.92 ppm
(f) d, δ 3.59 ppm (impurity, possibly thiocyanate)

J_{ae} = 4.7 Hz, J_{be} = 4.7 Hz, J_{ad} = 3.2 Hz, J_{cd} ◘ 1.5 Hz, J_{ce} ◘ 10 Hz, J_{de} = 17.5 Hz

Integration Ratios:

(a) } 1.82
(b) }
(c) } 2.00
(d) }
(e) 1.17
(f) 0.06

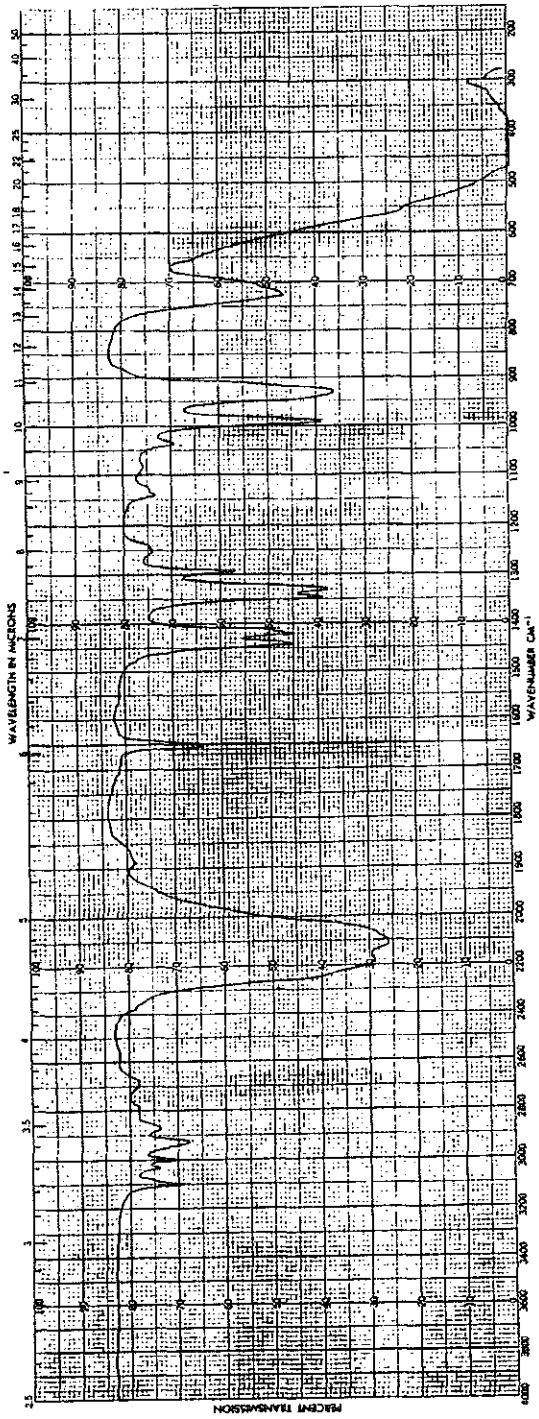

Figure 5. Infrared Absorption Spectrum of Allyl Isothiocyanate (Lot No. 532251)

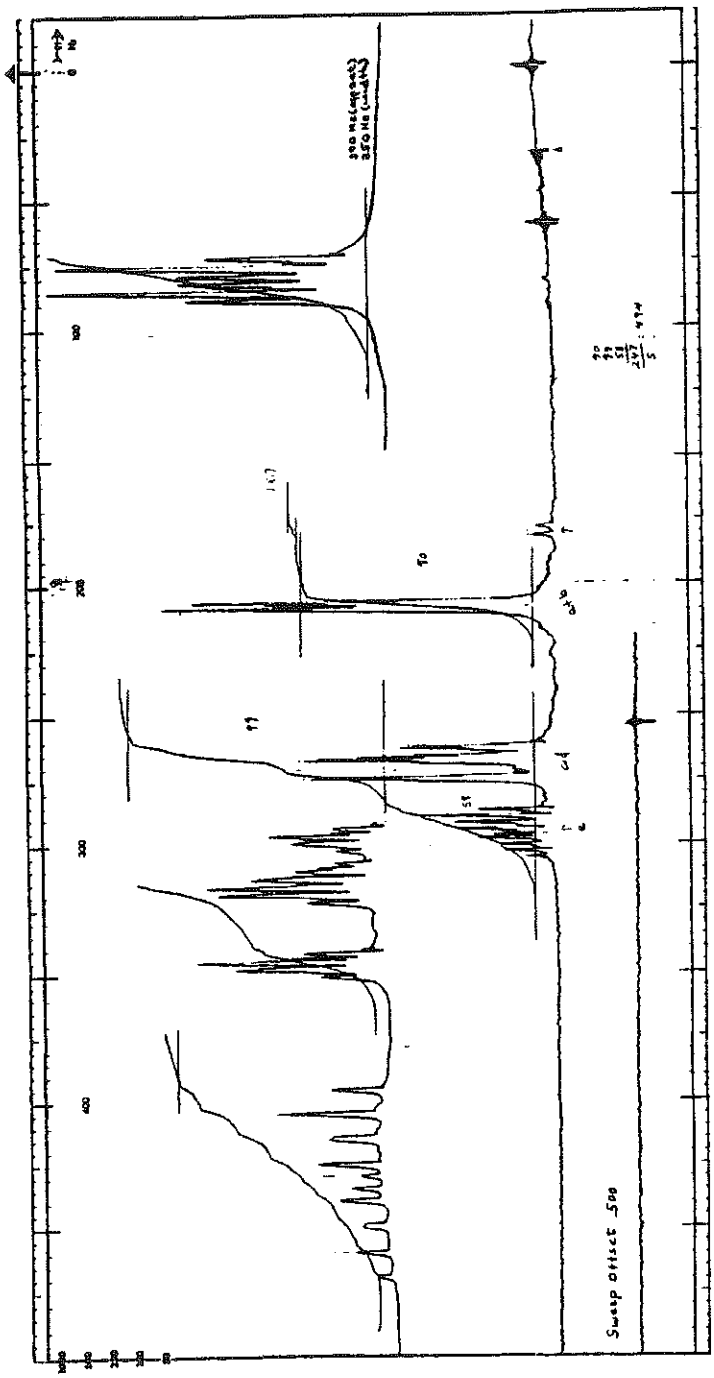

Figure 6. Nuclear Magnetic Resonance Spectrum of Allyl Isothiocyanate (Lot No. 532251)

APPENDIX F

ANALYSIS OF ALLYL ISOTHIOCYANATE IN CORN OIL FOR STABILITY OF ALLYL ISOTHIOCYANATE

APPENDIX F

A. PREPARATION OF SAMPLE AND STORAGE

A 26-μl aliquot of allyl isothiocyanate (26.90 mg) was placed in a 50-ml volumetric flask containing 50 ml corn oil, shaken, and placed in an ultrasonic vibrator bath for 30 seconds. The flask was stored at room temperature for 7 days with no effort made to protect the solution from light.

B. DILUTION AND ANALYSIS

1. Procedure

A 1.84-ml aliquot of the above stock solution (allyl isothiocyanate in corn oil) was pipetted into a small septum vial and 2 ml of anhydrous ethyl ether containing decane (15.63 mg decane in 50 ml ether) was added. The septum vial was sealed and mixed on a vortex mixer for 1 minute and placed in an ultrasonic vibrator bath for 2 minutes. The ether-corn oil mixture was analyzed by vapor-phase chromatography.

Note: Solvents which were immiscible with corn oil, such as alcohols, were not used due to their reactivity with allyl isothiocyanate. Therefore, dilution rather than extraction was used.

2. Instrumental Parameters

Instrument: Bendix 2500 with Hewlett-Packard 3380A automatic recorder/integrator
Detector: Flame ionization
Column: 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m × 4 mm I.D., glass
Oven temperature: 90°C, isothermal
Inlet temperature: 130°C
Detector temperature: 285°C
Carrier gas: Nitrogen
Carrier flow rate: 50 cc/min
Sample injected: 5 μl

C. QUALITY ASSURANCE PROCEDURES

Analysis was performed in duplicate using decane as an internal standard. Linearity studies were done at two concentration levels (0.26 mg/ml and 0.13 mg/ml or 0.026% and 0.013%) to determine the relative weight response of compound versus internal standard (decane).

D. RESULTS

Day	Theoretical Percent (Chemical/Vehicle)	Determined Percent (Chemical/Vehicle)	Percent D/T × 100
0	0.02578	0.02578 ± 0.00081	100 ± 3
1	0.02578	0.02656 ± 0.00039	103 ± 2
2	0.02578	0.02480 ± 0.00031	96 ± 1
3	0.02578	0.02533 ± 0.00025	98 ± 1
4	0.02578	0.02455 ± 0.00084	95 ± 3
7	0.02578	0.02566	99.54

Retention time: Compound (4.7 min.), internal standard (11.7 min.)
Response of allyl isothiocyanate in corn oil versus that of allyl isothiocyanate in ether: 93.1 ± 0.3%
Linearity: RWR $\frac{\text{compound}}{\text{internal standard}}$ = 0.70 ± 0.03 at two concentration levels (0.026% and 0.013%).

E. CONCLUSION

The variation in the analysis is within the error of the method. Therefore, allyl isothiocynate is stable in corn oil at 0.05% concentration when stored at room temperature for 7 days without protection from light.

APPENDIX G

ANALYSIS OF ALLYL ISOTHIOCYANATE IN CORN OIL FOR CONCENTRATIONS OF ALLYL ISOTHIOCYANATE

APPENDIX G

Allyl isothiocyanate in corn oil mixtures was analyzed directly by vapor-phase chromatography. Extractions were not performed on the samples since corn oil does not interfere with the analysis. Gas chromatography conditions were as follows:

Column:	3% OV-17 on 80/100 Supelcoport, 1.8 m x 2 mm I.D., glass
Detection:	Flame Ionization
Temperatures:	Inlet, 250°C Oven, 75°C, isothermal Detector, 275°C
Retention Time:	1.1 min.
Injection Size:	1 μl

There was no correction for work-up loss since samples were injected without any work-up. Reference samples of allyl isothiocyanate were prepared in corn oil and analyzed under the same conditions.

Results: See Table G1.

TABLE G1. ANALYSIS OF ALLYL ISOTHIOCYANATE IN CORN OIL FOR CONCENTRATIONS OF ALLYL ISOTHIOCYANATE

Date Mixed *(a)*	Used During Week of:	Concentration *(b)* of Allyl Isothiocyanate for Target Concentration of 0.12% (v/v)	0.24% (v/v)	0.25% (v/v)	0.50% (v/v)
04/10/78	04/11/78	0.10	0.23	0.25	0.48
05/05/78	05/06/78			0.25	0.48
06/07/78	06/08/78			0.25	0.48
07/05/78	07/06/78	0.12	0.24		
08/16/78	08/17/78			0.25	0.50
09/13/78	09/14/78	0.11	0.25		
10/11/78	10/12/78				0.50
11/09/78	11/10/78			0.24	
12/06/78	12/08/78				0.48
01/04/79	01/05/79			0.25	
02/01/79	02/02/79				0.47
03/01/79	03/02/79			0.25	
03/29/79	03/30/79				0.51
04/26/79	04/27/79			0.24	
05/24/79	05/25/79				0.53
06/21/79	06/22/79			0.24	
07/19/79	07/20/79				0.49
08/16/79	08/17/79			0.24	
09/13/79	09/14/79				0.46
10/11/79	10/12/79			0.24	
11/08/79	11/09/79				0.51
12/06/79	12/08/79			0.23	
01/03/80	01/04/80				0.51
02/01/80	02/02/80	0.11	0.26		
02/28/80	02/29/80			0.27	0.52
Mean (%)		0.11	0.25	0.25	0.49
Standard Deviation		0.01	0.01	0.01	0.02
Coefficient of variation (%)		9.1	4.0	4.0	2.0
Range (%)		0.10-0.12	0.23-0.26	0.23-0.27	0.46-0.53
Number of samples		4	4	13	14

(a) Start dates were March 1978 for rats and mice.
(b) The data presented are the average of duplicate analyses.

APPENDIX H

CUMULATIVE MEAN BODY WEIGHT CHANGE OF RATS AND MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE IN THE CHRONIC STUDY

TABLE H1. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males	0	133 *(b)*	134 *(b)*	133 *(b)*		
	5	115	115	108	0	- 6
	26	272	273	237	0	-13
	47	332	336	296	+ 1	-11
	79	337	345	324	+ 2	- 4
	104	317	326	298	+ 3	- 6
		450 *(c)*	460 *(c)*	431 *(c)*	+ 2 *(d)*	- 4 *(d)*
Females	0	99 *(b)*	102 *(b)*	100 *(b)*		
	5	48	51	50	+ 6	+ 4
	26	107	109	107	+ 2	0
	47	125	134	132	+ 7	+ 6
	79	166	184	180	+11	+ 8
	104	180	191	195	+ 6	+ 8
		279 *(c)*	293 *(c)*	295 *(c)*	+ 5 *(d)*	+ 6 *(d)*

(a) Weight change of the dosed group relative to that of the controls = $\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$

(b) Initial weight.

(c) Mean body weight at week 104.

(d) Mean body weight at week 104 relative to controls.

TABLE H2. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males	0	22 *(b)*	23 *(b)*	22 *(b)*		
	5	7	6	6	-14	-14
	26	20	19	21	- 5	+ 5
	47	26	23	28	-12	+ 8
	79	28	27	32	- 4	+14
	104	26	23	27	-12	+ 4
		48 *(c)*	46 *(c)*	49 *(c)*	- 4 *(d)*	+ 2 *(d)*
Females	0	17 *(b)*	18 *(b)*	18 *(b)*		
	5	7	5	5	-29	-29
	26	11	10	11	- 9	0
	47	14	13	16	- 7	+14
	79	18	19	19	+ 6	+ 6
	104	20	18	18	-10	-10
		37 *(c)*	36 *(c)*	36 *(c)*	- 3 *(d)*	- 3 *(d)*

(a) Weight change of the dosed group relative to that of the controls = $\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$

(b) Initial weight.

(c) Mean body weight at week 104.

(d) Mean body weight at week 104 relative to controls.

☆ U.S. GOVERNMENT PRINTING OFFICE: 1982-381-132:703

NIH Publication No. 83-1790
October 1982

NIH Publication No. 83-1790
October 1982