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Eye Irritation Study

In an eye irritation study conducted on rabbits using the technique of Draize, 0.1 ml of 50% Aqueous TRIS NITRO was placed in one eye of each of six rabbits. Only two of the rabbits showed mild redness of the conjunctivae and only one animal had a score of two at 24 hours. The eyes of all rabbits were normal for the remainder of the observation period.

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ENVIRONMENTAL CONSIDERATIONS

When properly used and disposed of, TRIS NITRO will have no measurable effect on the environment. As an antimicrobial agent for industrial applications, TRIS NITRO should never be released directly to the environment if materials containing it are properly handled. For example, cutting oils are harmful to fish and wildlife if released directly to water courses even if they do not contain TRIS NITRO. Such materials must always be treated physically, chemically, and/or biologically in industrial treatment systems to render them harmless before disposal.

TRIS NITRO provides protection from microbial contamination under alkaline conditions by decomposing to release formaldehyde. TRIS NITRO in any alkaline fluid will, in time, break down (see Figure 1). Even when a fluid has been treated a number of times, TRIS NITRO will not increase concentration in the system. Used cutting fluids, for example, will have much lower TRIS NITRO concentrations than when freshly prepared, and the remaining TRIS NITRO will degrade. A study has shown that low concentrations of TRIS NITRO are assimilated by sludge obtained from a municipal sewage system.

When properly handled and disposed of, TRIS NITRO will not be released directly to the environment. Nevertheless, studies have been conducted to assess the possible effects on wildlife which might result from improper handling or accidental spills of the compound.

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The 5-day dietary LC_{50} in mallard ducks was found to be in excess of 80,000 ppm of TRIS NITRO (expressed as the 50% solution). The LC_0 was in excess of 40,000 ppm. The symptoms of toxicity seen at doses of 20,000 ppm or more appeared to be reversible when the birds were fed an untreated diet for 16 days post-treatment. All birds were normal when fed 2500, 5000, or 10,000 ppm TRIS NITRO.

The 5-day dietary LC_{50} in bobwhite quail was found to be in excess of 5000 ppm of TRIS NITRO (expressed as the 50% solution). No symptoms suggestive of toxicity were seen in birds fed 1250, 2500, or 5000 ppm TRIS NITRO.

The LC_{50} of TRIS NITRO for rainbow trout was calculated at 410 ppm. This implies that TRIS NITRO Technical is practically nontoxic to trout.

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HANDLING AND STORAGE

TRIS NITRO 50% solution will crystallize if cooled below approximately 13°C (55°F). It is therefore recommended that care be taken during transit, and provision be made for such storage that TRIS NITRO 50% solution is maintained at temperatures slightly higher than 13°C (55°F).

TRIS NITRO solution which has become frozen may be thawed and used without any loss of potency. This is most conveniently and safely accomplished by placing the frozen material in a heated storage area and agitating the contents. If this is impractical, frozen TRIS NITRO solution can be thawed through the use of a hot water-bath and frequent agitation of the drum to mix the contents. Care should be taken that the temperature of the polyethylene drum liner is not allowed to exceed 75°C (167°F).

TRIS NITRO decomposes in the presence of alkaline materials, so it should be protected from vapors of ammonia and amines during handling and storage to prevent deterioration.

SHIPPING CONTAINERS

TRIS NITRO 50% aqueous solution is packaged in polyethylene bottles or in steel drums with polyethylene liner with net weights of 10 lb, 45 lb, and 500 lb.

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PRECAUTIONARY LABELING**CAUTION!**

Avoid contact with eyes.
Harmful if swallowed. Wash thoroughly with soap and water after handling and before eating or smoking.
Harmful if inhaled. Avoid breathing spray mist.
Remove contaminated clothing and wash before reuse.

STATEMENT OF PRACTICAL TREATMENT

- IF SWALLOWED:** Call a physician or Poison Control Center.
Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person.
- IF IN EYES:** Flush with plenty of water. Call a physician.
- IF ON SKIN:** Wash thoroughly with soap and water.
- IF INHALED:** Remove victim to fresh air. If not breathing, give artificial respiration and get medical attention.

ANGUS Chemical Company
assumes no responsibility when the product is not used in accordance with the instructions and information contained herein. It is a violation of federal law to use this product in a manner inconsistent with its labeling.

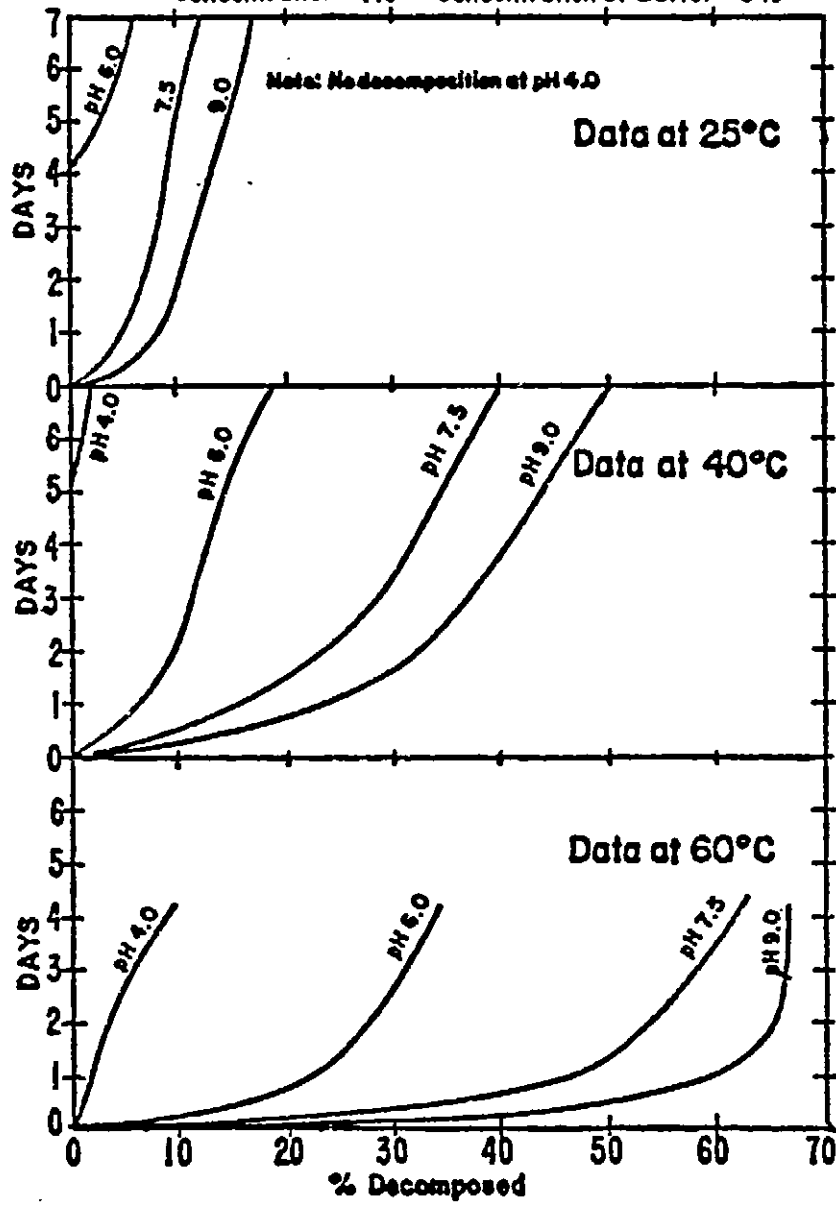
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FIG. 1

STABILITY OF TRIS NITRO IN PHOSPHATE BUFFER SOLUTIONS

Concentration = 1% Concentration of Buffer = 5%



ACCEPTED
with COMMENTS
in EPA Letter Dated:

NOV 29 1962

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.

48301-4

29 NOV 1982

Angus Chemical Co.
2211 Sanders Road
Northbrook, IL 60062

Attention: Mr. Allen E. Bollmeier, Jr.

Gentlemen:

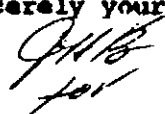
Subject: Tris Nitro Aqueous For Formulating Use
EPA Registration No. 48301-4
Your Application Dated September 22, 1982

The proposed data brochure and label, submitted in connection with registration under FIFRA, are acceptable provided that you:

1. Make the labeling changes listed below before you release the product for shipment.
 - a. The Data Brochure must contain the correct/current EPA Registration Number 48301-4.
2. Submit five (5) copies of your final printed labeling before you release the product for shipment.
3. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA sec. 6(e). Your release for shipment of the product bearing the amended labeling constitutes acceptance of these conditions.

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

Sincerely yours,



John H. Lee
Product Manager (31)
Disinfectants Branch
Registration Division (TS-767C)

Enclosure

TS-767C:Lee:DCR-55774:WANG-1144C:hk:Raven:479-2013:11/15/82

TRIS NITRO® BRAND OF 50% AQUEOUS TRIS(HYDROXYMETHYL)NITROMETHANE
BACTERIOSTAT FOR FORMULATING END-USE PRODUCTS
FOR INDUSTRIAL USE

ACTIVE INGREDIENT:
2-Hydroxymethyl-2-nitro-1,3-propanediol 50%
INERT INGREDIENTS: 50%
..... 100%

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

CAUTION!

AVOID CONTACT WITH EYES.
HARMFUL IF SWALLOWED. WASH THOROUGHLY WITH SOAP
AND WATER AFTER HANDLING AND BEFORE EATING
OR SMOKING.
HARMFUL IF INHALED. AVOID BREATHING SPRAY MIST.
REMOVE CONTAMINATED CLOTHING AND WASH BEFORE
REUSE.

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.

ACCEPTED
with COMMENTS
EPA Letter Dated
48301-4
NOV 29 1982

STATEMENT OF PRACTICAL TREATMENT

IF SWALLOWED: Call a physician or Poison Control Center. Drink 1 or 2 glasses of
water and induce vomiting by touching back of throat with finger. Do not induce
vomiting or give anything by mouth to an unconscious person.
IF IN EYES: Flush with plenty of water. Call a physician.
IF ON SKIN: Wash thoroughly with soap and water.
IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration
and get medical attention.

ENVIRONMENTAL HAZARDS

Do not contaminate water by cleaning of equipment or disposal of
wastes. Do not discharge into lakes, streams, ponds, or public water
unless in accordance with the NPDES permit. For guidance, contact
your Regional Office of the EPA.

ANGUS Chemical Company assumes no responsibility when this product is not used
in accordance with the instructions and information contained on this label.

STORAGE AND DISPOSAL

STORAGE: Freezes at 60°F.

Store in a warm place.

TRIS NITRO decomposes in the presence of alkaline materials. Protect
from vapors of ammonia and amines during handling and storage to prevent
deterioration and release of formaldehyde.

DISPOSAL: Do not contaminate water, food, or feed by storage or disposal. Open
dumping is prohibited. Pesticide or rinsate that cannot be used or chemically
reprocessed should be disposed of in a landfill approved for pesticides. Triple
rinse (or equivalent) all containers. Then offer for recycling or reconditioning, or
puncture and dispose of in a sanitary landfill or by other approved state and local
procedures.

INSTRUCTIONS FOR FORMULATION

It is a violation of Federal law to use this product in a manner inconsistent with its
labeling.

This pesticide may be used only for formulation of an industrial bacteriostat.

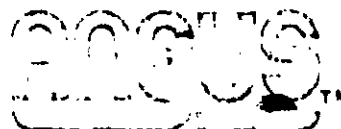
Formulators using this product are responsible for obtaining EPA registration for
their formulated products. Refer to NP Technical Data Sheet for formulating and
other information.

See Additional Precautionary Statements on Side Panel and in Technical Bulletin.

E.P.A. Reg. No. 48301-4AA

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Printed in U.S.A.



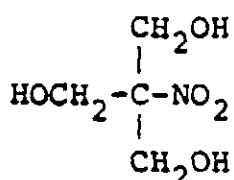
ANGUS Chemical Company
221 Sanders Road
Northbrook, IL 60062

Proposed
Data Sheet

ACCEPTED
with COMMENTS
in EPA Letter Dated:

NOV 29 1982

Under the Federal Insecticide,
Fungicide, and Rodenticide Act
as amended, for the pesticide
registered under EPA Reg. No.
48501-4



TRIS NITRO® BRAND OF 50% AQUEOUS
Tris(hydroxymethyl)nitromethane*

EPA Reg. No. 271-26

TRIS NITRO is an antimicrobial agent particularly suited for the control of bacteria and slimes in industrial applications. It is available as a 50% aqueous solution of tris(hydroxymethyl)nitromethane.

Purified TRIS NITRO is a white crystalline solid which is quite stable when dry. At its melting point crystalline TRIS NITRO decomposes slowly, but there is no tendency for this decomposition to become self-sustaining because the reaction is endothermic.

TRIS NITRO is highly soluble in water and is quite stable in neutral or weakly acidic solution. However, in slightly alkaline solution TRIS NITRO slowly decomposes to release formaldehyde. Formaldehyde is released more rapidly as pH is increased. This release can be easily controlled by pH adjustment and/or temperature so that the working life of TRIS NITRO can be varied from a few minutes to several months according to conditions of use (See Figure 1).

* Indexed by *Chemical Abstracts* as 2-hydroxymethyl-2-nitro-1,3-propanediol, CAS Registry No. 126-11-4.

TRIS NITRO is a trademark of International Minerals & Chemical Corporation.

Physical Properties of Pure
Tris(hydroxymethyl)nitromethane

Molecular weight (calculated)	151.124
Melting point (melts with decomposition)	175-176°C
pH of 0.1M aqueous solution at 20°C	5.0
Critical humidity point at 40°C	66% R.H.
Solubility in water at 20°C	220 g/100 ml

Very soluble in alcohols; insoluble in hydrocarbons
such as heptane, diisobutylene, kerosene, styrene,
mineral oil, benzene, toluene.

Typical Physical Properties of the 50% Aqueous Solution

Crystallization point (approx.)	55°F
Specific gravity at 25/25°C	1.222

Specifications of the 50% Aqueous Solution

TRIS NITRO, % by wt	50 (min.)
Free formaldehyde, % by wt	1 (max.)
pH, as is	2.0-4.5
Color, Gardner	5.0 (max.)

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ANTIMICROBIAL ACTIVITY

Although some antimicrobial activity is provided by TRIS NITRO at a pH as low as 6, it is most effective at pH 7.5 or higher where there is a gradual release of formaldehyde to provide continuous activity for a prolonged period. Under ordinary use conditions the odor of formaldehyde should not be detectable.

The antimicrobial effectiveness of TRIS NITRO against many organisms is indicated by the following spectrum. Repeated transfers have been made with many of these organisms without any indications of a tendency to develop resistance.

The following information is intended only to indicate the broad-spectrum activity of the product. This information must not be interpreted as having relevance to the use pattern recommended, effective dosages, activity against specific microorganisms, or any other implications of effectiveness of formulated products.

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ANTIMICROBIAL SPECTRUM OF TRIS NITRO

<u>Organism</u>	Minimum Inhibitory Concentration
	at pH 7.4
	of 50% Aqueous TRIS NITRO as supplied
<i>Bacillus subtilis</i>	250-500 ppm
<i>Staphylococcus aureus</i>	65-125
<i>Streptococcus faecalis</i>	250-500
<i>Sarcina lutea</i>	125-250
<i>Escherichia coli</i>	500-1000
<i>Aerobacter aerogenes</i>	65-125
<i>Pseudomonas aeruginosa</i>	500-1000
<i>Salmonella typhi</i>	65-125
<i>Desulfovibrio aestuarii</i>	<33
<i>Cladosporium herbarum</i>	>2000
<i>Cephalosporium species</i>	1000-2000
<i>Trichophyton mentagrophytes</i>	250-500
<i>Aspergillus niger</i>	>2000
<i>Aureobasidium pullulans</i>	>2000
<i>Fusarium moniliforme</i>	>2000
<i>Saccharomyces cerevisiae</i>	500-1000
<i>Candida albicans</i>	>2000

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Many industrial operations involve the recirculation of fluids (water, oil, or emulsions) which are subject to contamination by microbes. These fluids provide an environment favorable to the growth and multiplication of microorganisms. Such growth, if unchecked, can lead to:

- 1) Foul odor.
- 2) Emulsion breakdown.
- 3) Acidification of the fluid, which in turn can cause corrosion problems.
- 4) Clogged pumps, valves, and filters.

Water Treatment

TRIS NITRO is effective against those microorganisms such as slimes which cause problems in industrial water systems. It is recommended for use in cooling-tower systems. However, since the conditions of use would vary greatly, use recommendations will depend on the nature of the specific system.

Metalworking Fluids

TRIS NITRO is an effective antimicrobial agent for the protection of metalworking fluids, i.e., cutting fluids and coolants for grinding and tooling operations. It has been shown to be effective in petroleum-based products, synthetic coolants, and semisynthetic fluids, such as those containing mineral oils, fatty oils, sulfurized fatty-mineral oil blends, sulfurized-chlorinated fatty-mineral oil blends, emulsifiable oils, glycols, or glycol-polyol esters.

Studies have demonstrated that 0.1% TRIS NITRO in a cutting oil formulation completely inhibited the growth of bacteria in the oil for a period of 60 days under conditions of optimum bacterial growth, and was more effective than over 200 compounds tested.

In another study 500 ppm of 50% aqueous TRIS NITRO was utilized to protect six different cutting fluids. Portions of these protected fluids were inoculated once a week with an inoculum containing bacteria and molds. The organisms in the inoculum, obtained from spoiled industrial cutting fluids, included pseudomonads, *Paracolocbactrum*, *Proteus*, and *Klebsiella* species, together with molds such as *Fusarium*, *Cephalosporium*, *Candida*, and *Monilia*. The results were as follows:

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	<u>Days of Inhibition</u>	
	<u>Unprotected Control</u>	<u>TRIS NITRO, 500 ppm</u>
Petroleum coolant #1	0	49
Petroleum coolant #2	0	63
Synthetic coolant #1	0	42*
Synthetic coolant #2	0	35
Semisynthetic coolant #1	0	49
Semisynthetic coolant #2	0	70

* Failure due to molds

Oilfield Flooding

Unchecked growth of sulfate-reducing bacteria in oilfield flooding applications can lead to plugging and serious corrosion problems. Laboratory tests indicate that as little as 50-100 ppm of TRIS NITRO in the water is sufficient to inhibit these bacteria.

Deodorizing Applications

TRIS NITRO is recommended as a component of deodorizing formulations such as those used in chemical toilets. Its controllable formaldehyde-releasing action eliminates odor problems associated with raw formaldehyde, and allows the formulator more latitude in choice of reodorants. TRIS NITRO is highly compatible with other deodorizers and sequestrants commonly used in these applications.

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Preservative for Packaged Emulsions,
Solutions, or Suspensions

TRIS NITRO is an excellent alternative to formalin as a preservative for protection of emulsions, solutions, or suspensions from deterioration. The amount of TRIS NITRO required for protection will vary with the type of product and the level of microbial contamination. For example, 500 ppm of active TRIS NITRO provided complete protection to a mineral oil emulsion throughout a 6-week study involving weekly inoculations with a mixed bacterial inoculum containing 10^7 organisms per milliliter.

DRILLING MUDS

Drilling muds contain surfactants, carboxymethyl-cellulose, and other ingredients susceptible to attack by microorganisms, and therefore they must be protected. TRIS NITRO is effective for the control of those microorganisms commonly encountered in this application. Use levels will vary with the degree of contamination, but in general levels effective in cutting oils will be effective in drilling muds.

Manufacturing Use in Formulated
Antimicrobial Products

TRIS NITRO is an excellent active ingredient for the formulation of spray fumigants and other antimicrobial products. The TRIS NITRO in such products slowly decomposes to release formaldehyde. Properly formulated products should be buffered to insure that this release of formaldehyde does not occur until dilution by the end-user of the product. Manufacturers of such products are responsible for obtaining registration of their formulated products with EPA under provisions of the Federal Insecticide, Fungicide, and Rodenticide Act.

TRIS NITRO is effective as an antimicrobial agent because it slowly decomposes to release formaldehyde. Incorporation into a metalworking fluid concentrate may lead to premature decomposition and loss of potency. It therefore should be added to the cutting oil, cooling system, etc. only when the fluid is actually in service. It may be used as part of an initial antimicrobial package and/or as an additive for the maintenance of protection as the fluid ages.

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It is possible to incorporate TRIS NITRO into a concentrate package as for chemical toilets provided care is taken to buffer the system to acid pH. Dilution at the time such packages are placed in use will shift the pH to the basic side and allow TRIS NITRO to function as a formaldehyde donor. Such systems must be carefully balanced to insure compatability and package stability of the various components.

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TOXICITYAcute Oral Animal Studies

A seven-day study on TRIS NITRO crystals given by gavage was conducted in mice with the following results:

LD ₀	1000 mg/kg
LD ₅₀	1900 ± 350 mg/kg
LD ₁₀₀	3000 mg/kg

In a similar 14-day study of 50% aqueous TRIS NITRO in rats, the LD₅₀ was determined to be 1875 mg/kg.

Intraperitoneal Study in Mice

In a seven-day study in mice TRIS NITRO crystals gave the following results by the intraperitoneal route:

LD ₀	1000 mg/kg
LD ₅₀	1850 ± 340 mg/kg
LD ₁₀₀	3000 mg/kg

Skin Irritation Studies

In another study, TRIS NITRO 50% aqueous diluted with distilled water to 1000 ppm, 3000 ppm, and 10,000 ppm active ingredient in water was applied to the skin of six rabbits. No skin irritation was observed for any of the exposed animals after 24 hours exposure.

A series of 48-hour patch tests was conducted by an independent dermatologist on 25 human volunteers using TRIS NITRO at concentrations of 0.3% and 0.6% in some typical cutting-oil emulsions. Another group was exposed to the cutting oil alone without TRIS NITRO. The tests were severe in that they were conducted with concentrations of TRIS NITRO considerably higher than any that have been found necessary to protect the emulsions from bacterial contamination. Both the closed and open methods of application were employed. The closed method insures maximal contact of the preparation with the skin and minimal loss by evaporation or wiping on the subject's clothing. There was absolutely no skin irritation in either the open or closed tests on any of the 25 subjects.

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In order to check on the sensitizing potential of aged cutting-oil emulsions containing TRIS NITRO, a series of human patch tests was conducted by another independent organization. The subjects were housewives, 30-65 years of age. The tests consisted of three successive patch exposures of 24 hours duration with 24 hours or more between exposures. The three compositions employed consisted of (a) a typical cutting-oil emulsion without TRIS NITRO, (b) the same emulsion to which 0.5% TRIS NITRO had been added just before use in the test, (c) the same emulsion to which 0.5% TRIS NITRO had been added some time previously so that aging effects would have had ample opportunity to develop. The results of this test showed that addition of 0.5% TRIS NITRO (five to ten times as much as normally used) caused no increase in irritating effect whether it was added just before use or some time previously. The dermatologist concluded that normal users of the emulsions would not be expected to experience any primary irritation under the usual conditions of use.

These findings are ample evidence that TRIS NITRO is not a primary irritant and that the sensitizing potential is minimal. A small but significant proportion of workers exposed to cutting oils in the metalworking industry experience dermatitis from diverse causes. Some cutting oils containing TRIS NITRO may be involved in a fraction of these cases due to some chemical reaction which is not understood, but which may occur over a long period of time.