CIRS Compagnia Italiana Ricerca e Sviluppo srl

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Technical dossier for FDA

# NOXOL WSW / ETH

## Antiscaling Agent in the polymerization of Polyvinylchloride (PVC) and acrylic polymers (indirect food additive petition)

## Re no.: 3B4380

## ENVIRONMENTAL ASSESSMENT

**Petition control branch**
**Food and Drug Administration**
**Department of health and human services**
**Washington DC 20204**

**Date: May 24th, 1995**

## NON CONFIDENTIAL SECTION

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## 0. Foreword

This Environmental Assessment corrects and substitutes the EA of March 8th, 1995 Re no. 3B4380.

List of changes:

| Edition | Item | Variation |
|---|---|---|
| September 8th, 1993 | | First edition |
| March 8th, 1995 | 5.1 | The C.A.S. number is no more in the confidential section. |
| | 5.4 | The molecular formula is no more in the confidential section. |
| | 5.7 | See confidential section |
| | 5.8 | See confidential section |
| | 5.10 | The composition was corrected by adding the sodium hydrosulfite |
| | 6.1 | In the **confidential section** there are more legislative and technological information about the production site, the workplace and the handling of raw materials. |
| | 9. | The points A, B and C have been rewritten for better comprehension |
| | 12. | The qualification and expertise of the person who prepared this dossier have been added. |
| | 14 | The Material Safety Data Sheet of NOXOL WSW and ETH has been added in the appendices. |
| | | **NOTE: all enclosures of former Environmental Assessment are still valid.** |
| | | The whole book has been re-edited to correct errors and improve comprehension 000583 |
| May 24th, 1995 | List of changes | "5.10 .....Sodium bisulfite" was replaced with "5.10 .....Sodium hydrosulfite" |
| | 5.10 | "Sodium bisulfite (CAS n. 7631-90-5)" was replaced with "Sodium hydrosulfite (CAS n. 7775-14-6)". 000583 |

**1. Date**

May 24th, 1995

**2. Name of petitioner**

C.I.R.S. (Compagnia Italiana Ricerca e Sviluppo) S.r.l.

**3. Address**

Località Colafonda - 45010 Cavanella Po - Rovigo - ITALY

**4. Description of proposed action**

NOXOL is intended to be used as an antiscaling agent in the polymerization of PVC and acrylic polymers.
At present NOXOL is produced at CIRS plant in Cavanella Po. NOXOL will be used in all processes of PVC and Acrylic polymerization, such as emulsion, suspension and bulk.
For this purpose the solution of NOXOL (NOXOL WSW or NOXOL ETH) is injected by steam into the reactor before the polymerization. In this way a film of NOXOL is formed on the walls of reactor. This film avoid the build up.

This use makes NOXOL an indirect food additive because some product may remain incorporated in the PVC or in the acrylic polymers. The requested approval is for the use of NOXOL in the manufacturing of PVC or acrylic polymers which may be used for the manufacturing of plastic materials intended to be in contact with water or aqueous solutions.

**4.1** Production site:

At present NOXOL is produced only at CIRS factory which is located in CAVANELLA PO - Rovigo - ITALY.
The factory is situated in a industrial area and it is 5 km from the nearest town (ADRIA).

**4.2** Location where the product will be used:

The sites where the product will be used are factories in which polymerization plants have been constructed.
These factories are usually complex installations where appropriate facilities for the disposal of waste water or materials are available.

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**4.3** Manufacturing of food packaging materials:

The plastic materials which are prepared with of NOXOL could be used for the manufacturing of articles, e.g. bottles, intended to be in contact with water or aqueous food stuffs.

## 5. Identification of chemical substances that are subject of the proposed action.

**5.1** Chemical name:

Poly (1-hydroxynaphtylmethane)

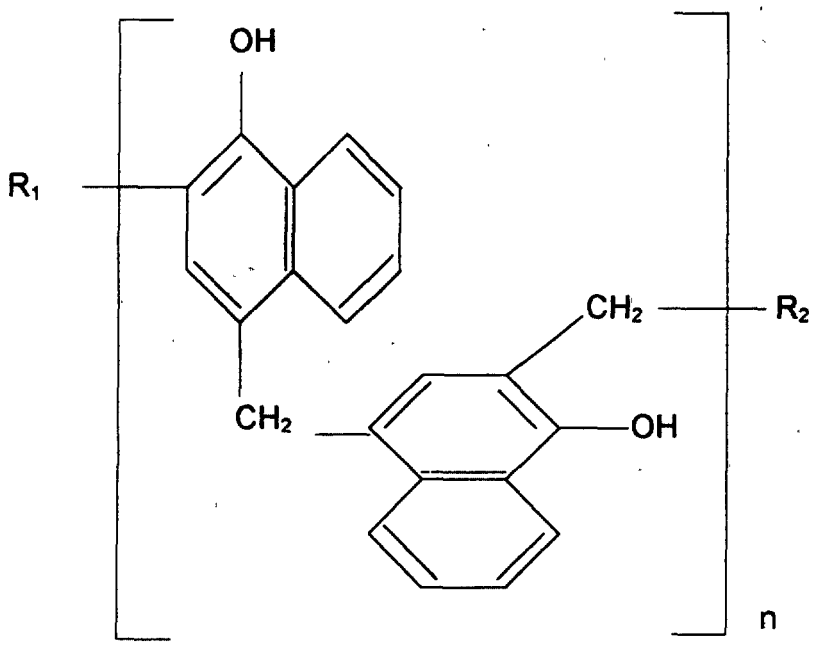
**5.2** CAS Registry Number:

25359-91-5

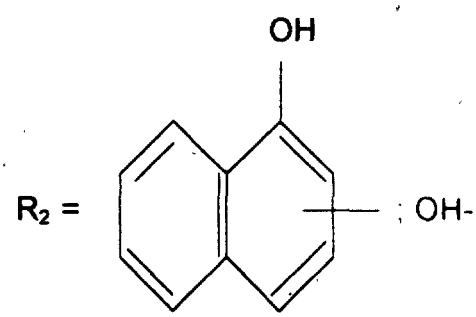
**5.3** Trade name:

NOXOL WSW (formulation in water)
NOXOL ETH (formulation in ethyl alcohol)

**5.4** Molecular and structural formula:




$R_1$ = H ; $-CH_2OH$

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**5.5** Molecular weight distribution:

The molecular weight distribution has been determined by Gel Permeation Chromatography (see annex A.4)

| MW | % |
|---|---|
| < 500 | 9.8 |
| 500/1000 | 37.2 |
| 1000/2000 | 49.0 |

**5.6** Physical-chemical data:

I.R. spectrum: (see annex A.5)
Melting point (glass transition): 170°C
Decomposition temperature (DSC): 280°C

Solubility at 20°C in:

| Solvent | g/l |
|---|---|
| Tetrahydrofuran | 1 |
| Acetone | 0.1 |
| Water | < 0.01 |
| Water at pH 12 | 80 |
| Octal | 0.4 |

**5.7** Manufacturing process:

(See confidential section)

**5.8** Purity:

> 98%

Impurities: (See confidential section)

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**5.9** Stability:

NOXOL is sensitive to the contact with the air; the solution by contact with the air changes colour from yellowish to greenish or bluish-black, depending on the duration of the exposure.

This process can be delayed by nitrogen fluxing.

Due to the extremely low concentration of the additive, this changing of colour has never been observed in plastic materials.

**5.10** Composition of the formulations:

| **NOXOL WSW** | **% (w/w)** |
|---|---|
| Active ingredient | 5 +/- 1 |
| Sodium hydroxide (CAS n. 1310-73-2) | 0.7 +/- 0.15 |
| Polyvinyl alcohols (CAS n. 9002-89-5) | 0.3 +/- 0.15 |
| Sodium hydrosulfite (CAS n.7775-14-6) | 0.2 +/- 0.1 |
| Water | 94 +/- 1 |
| **NOXOL ETH** | |
| Active ingredient | 21 +/- 2 |
| Sodium hydroxide (CAS n. 1310-73-2) | 3 +/- 0.3 |
| Ethanol (CAS n. 64-17-5) | 11 +/- 1 |
| Sodium hydrosulfite (CAS n.7775-14-6) | 0.2 +/- 0.1 |
| Water | 65 +/- 2 |

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## 6. Introduction of substances into the environment

### 6.1 Location where the product will be used

NOXOL is produced in a closed system. During the manufacturing process, there is any dangerous exposure in the work place and since all the reaction mass is used to prepare the solutions of NOXOL in water (NOXOL WSW) or in water-ethanol (NOXOL ETH) there is not production of either waste water or gaseous emissions.

See 6.1 in the Confidential Section for more information on the treatment of the emissions and on the relevant Italian and European legislation.

See the Safety Data Sheet of NOXOL WSW and NOXOL ETH in Annex 6.1.

### 6.2 Location where the product will be used

As explained before, the solutions of NOXOL are injected by steam in closed reactors in order to obtain the expected antiscaling effect. Part of the product remains on the reactor walls, but most of it is discharged, as sludge, with the mother and the washing waters. During this phase there is not dangerous exposure in the work place.

Regarding the final destination of NOXOL in the waste waters, we know that NOXOL is not very biodegradable, but due to his physical and chemical properties, by dilution at neutral pH it forms sludge which can be easily separate from the waste waters.

The plants for the production of PVC or acrylic polymers are usually located in large factories where appropriate waste treatments are available.

In conclusion, of 100 kg of NOXOL Active Substance 25 Kg may become a non-functional component of the finished food packaging materials. These data are estimated in excess since they do not consider the NOXOL remaining on the reactor walls. 75 kg go to the waste water of the polymerization site.

### 6.3 Food packaging materials, manufacturing and disposal

The PVC packaging materials which will be in contact with foodstuffs, are articles intended to be in contact with water or aqueous solutions (e.g., bottles for mineral water).

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Due to their extremely low content of NOXOL there are not problems for their disposal, or incineration, or recycle according to the usual systems.

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## 6.4 Yearly market

In the following table you will find:
- the estimate market of NOXOL (100% active substance);
- the percentage of product that will be used for plastics intended to be in contact with foodstuff;
- the percentage of product that will become a non-functional component of finished food packaging materials.

Potential market

| | Year | 1995 | 1996 | 1997 |
|---|---|---|---|---|
| 1 | Total production NOXOL 100% a.s. | 48 tons | 55 tons | 60 tons |
| 2 | NOXOL used for plastics intended to be in contact with foodstuffs | 10%<br>4.8 tons | 10%<br>5.5 tons | 10%<br>6.0 tons |
| 3 | NOXOL as a non-functional component of packaging materials | 25%<br>1.2 tons | 25%<br>1.37 tons | 25%<br>1.5 tons |
| 4 | NOXOL in the U.S.A market | 25%<br>12 tons | 30%<br>13.7 tons | 35%<br>15 tons |

The data in the third line of the table have been determined as follows:

| | | |
|---|---|---|
| a) | NOXOL WSW or ETH sprayed onto the reactor internal walls | 3.6 g/ton of VCM |
| b) | NOXOL WSW or ETH discharged from the reactor during the washing with water after the application | 2.7 g/ton of VCM (75% of sprayed NOXOL) |
| c) | NOXOL WSW or ETH applied onto the internal walls of the reactor as an antiscaling agent | 0.9 g/ton of VCM (0.00009 % of PVC product) |
| d) | NOXOL WSW or ETH removed from the reactor after 100 polymerization cycles, by washing it at the pressure of about 200 bar | about 0.9 g/ton of VCM<br><br>(This analytical datum is very approximate) |

As you can observe, the quantity of NOXOL which may remain as a non-functional component has been estimated without considering the quantity remaining on the walls. The data reported in (d) are information supplied by CIRS customers.

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## 7. Fate of the emitted substances

### 7.1 Physical chemical product data:

| | |
|---|---|
| Water- solubility | < 0.01 g/l at 20°C |
| Octanol solubility | 0.04 g/l at 20°C |
| Vapour pressure | Not applicable: NOXOL is a polymer |
| Dissociation constant | Not applicable: NOXOL is a polymer |
| Melting point (glass transition) | 170°C |
| Decomposition temperature (DSC) | 280°C |
| Photodegradation | no evidence |

### 7.2 Aerobic biodegradation in water:

Not readily biodegradable; it does not display inhibitory effects (Annex 7.2)

### 7.3 Air:

NOXOL is a polymer with average M.W. 1,292 g/mol, and for this reason it is reasonable to exclude its volatilization.

NOXOL is sensitive to the contact with the air: the solution, by contact with the air, changes colour from yellowish to greenish or bluish black, depending on the duration of the exposure. This phenomenon has never been observed in plastics prepared with NOXOL.

### 7.4 Aerobic biodegradation in the soil:

NOXOL is not supposed to get in contact with the soil, unless accidental events occur.

### 7.4 Migration data:

The migration of NOXOL from PVC to water is < 0.005 mg/Kg (see annex D. 1.4).

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## 8. Environmental effects of released substances

According to EEC Directives, given a specific migration lower than 0.05 mg/Kg of food simulator, the toxicological tests are as follows:

### 8.1 Genotoxicity

#### 8.1.1 Gene mutation in bacteria:

Ames test: the test was carried out with S. typhimirium (TA 1535, TA 1538, TA 98 and TA 100):

E. Coli test WP2: reversion test was carried out with E. Coli; the elements used are WP2, WP2uvrA and PKM101.

#### 8.1.2 Citotoxicity with CHO cells from Chinese hamster's ovary:

Results and comments

mutagenic action: from the two tests no toxicity or genotoxical action in any of the elements used in the tests has been pointed out.

citotoxicity: with the tested concentrations the results were similar, with or without S-9 mix. Only in the highest concentration that as been tested (10 mg/ml) high citotoxicity has been observed.

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**8.1.3** Gene mutation in cultured mammalian cells:

Under the experimental conditions applied, the overall results indicate absence of mutagenicity of the product NOXOL WSW in V79 Chinese hamster's lung cells, whether in presence or in absence of metabolic activation,

Preliminary Toxicity test

A preliminary toxicity test was carried out at the dosage of 10, 100, 1000, 2500 and 5000 µg/ml. The test substance proved to be cytotoxic at the highest dosage, both in presence or in absence of metabolic activation. At the dosage level of 2500 µg/ml the plating efficiencies[1] were 59% and 71% in the test, without and with metabolic activation respectively.

Furthermore, at these doses precipitation of the test substance in the incubation mixture occurred.

Gene mutation in V79 Cells

The protocol for mutagenicity study provides two independent experiments. As concerns the second experiment, in the test with metabolic activation a significant increase in mutant frequency in comparison with the control was observed in the cells treated with NOXOL WSW at the dose of 1000 µg/ml. For this reason, two more experiments were carried out in order to better investigate the genotoxicity on the test system.

The third test was not evaluated because pollution occurred in most of the plates.

A fourth experiment was carried out successfully and the results were negative.

The increase observed in the second experiment cannot be considered indicative of mutagenic activity, since it was not confirmed in the other two independent experiments.

**8.1.4** Acute oral toxicity

LD50 oral rat: > 5000 mg/Kg (test limit).

**NOTE**: All the tests were carried out according to the OECD and EEC regulations. The reports of the tests are in Annex E.1

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[1] Plating efficiency % = (mean number of colonies grown in non selective medium plate) / (number of seeded cells) x 100

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## 9. Use of resources and Energy

NOXOL is produced and commercialized for a sole and unique use upon precise request of the producers of Suspension and Emulsion PVC and acrylic polymers.

As an antiscaling agent, NOXOL has been studied to substitute the antiscaling agents which are used by industries and which consist of ammoniacal (Nigrosine) or polyphenolic substances, that are notoriously toxic and of difficult application.

NOXOL, therefore is not introduced in the market with the aim at increasing the production or reducing the costs of production, but for the following three precise reasons:

a) to maintain reactor walls clean for a long time and to avoid the opening of reactors so that the pollution with toxic gaseous vinyl chloride monomer is reduced;

b) to use an antiscaling agent with irrelevant migration data and without any negative effect on PVC and acrylic polymers;

c) to have a product without any negative effects on waste water.

In conclusion, NOXOL does not directly affect the volumes and costs of production of PVC Polymers, while it offers a solution in order to avoid the frequent opening of reactors (which is the purpose of the Closed Manhole Technology) and eliminate the use of a large number of not acceptable substances that now all companies are forced to use.

## 10. Mitigation measures

On the basis of the above-stated data and on the basis of CIRS and its Customers' experiences, CIRS declares that no particular negative environmental effects have been identified so that no particular measures to avoid or mitigate negative environmental impact are requested.

## 11. Alternative to the proposed action

On the basis of the above-stated data and on the basis of CIRS and its Customers' experiences, CIRS declares that no particular negative environmental effects have been identified so that no alternative actions can be proposed.

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## 12. List of preparers

This dossier has been written out by:

Dr Antonio Quattrini

1972 - 1982 Responsible for Pilot Plant of Dow-Lepetit Italy. In this position he had the opportunity to prepare parts of dossiers for the registration of new drugs.

1982 - 1990 Responsible for Regulatory affairs in ENICHEM Synthesis, for the introduction on the market of new chemicals and the registration of pesticides.

1990 - CIRS Responsible for Regulatory Affairs, Quality Assurance and Environment.

Consultant:

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1730 Rhode Island Avenue, NW. 907
Washington, D.C. 20036

## 13. Certification

The undersigned official certifies that the information presented is true, accurate, and complete to the best of the knowledge of firm responsible for the preparation of the environmental assessment.

Date: May 24th, 1995

Mr. Francesco Carlin

C.I.R.S. President

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## 14. Appendices

| | |
|---|---|
| ANNEX A.4 | Molecular Weight Distribution |
| ANNEX A.5 | IR Absorption Spectrum |
| ANNEX 7.2 | Aerobic Biodegradation in water |
| ANNEX D.1.4 | Migration Data |
| ANNEX E.1 | Toxicological Data |
| ANNEX 6.1 | Material Safety Data Sheet<br>NOXOL WSW<br>NOXOL ETH |

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