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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES
OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505C)

DEC 20 2005

DECISION MEMORANDUM

SUBJECT: Registration of Polyxylenol Tetrasulfide (PXTS)

FROM: Frank Sanders, Director
Antimicrobials Division (7510C)

TO: James J. Jones, Director
Office of Pesticide Programs (7501C)

I. CHEMICAL AND APPLICATION INFORMATION

REGISTRANTS: Akzo Nobel Functional Chemicals, LLC

CHEMICAL: Polyxylenol Tetrasulfide (PXTS)

PRODUCTS: Products include the technical product and one end-use product

PRODUCT NAMES: Technical: Verigard Technical 75799-1 (80.5 % MUP)
End use: Verigard Blend D 75799-2 (53.9%)

USE: Pressure and thermal treatment of wood products for use in commercial/industrial settings such as utility poles, railroad ties and products used in an aquatic environment (pilings etc.).

REGISTRATION TYPE: Conditional Registration

II. HIGHLIGHTS OF SCIENCE REVIEWS

A. TOXICOLOGY

1. ACUTE TOXICITY

Technical polyxylenol tetrasulfide is toxicity category IV for oral, dermal toxicity, dermal irritation and inhalation toxicity and is not a dermal sensitizer. Technical polyxylenol tetrasulfide is toxicity category III for eye irritation.

2. DEVELOPMENTAL/REPRODUCTIVE TOXICITY

Polyxylenol tetrasulfide shows no significant reproductive effects. In a rat reproductive/developmental screening toxicity study, no reproductive toxicity was observed at any dose. Significantly decreased pup weight was noted in the mid- and high-dose groups. At the high dose (500 mg/kg/day) a significant increase in the mean number of pup deaths and a significant decrease in pup survival were observed. Treatment-related clinical observations were noted in parental animals at the high dose including salivation, discoloration around the mouth, redness around the nose fur, rough coat, discolored paws, coldness to the touch and hunched posture. Enlarged spleens were observed in parental animals as well at all dose levels (mid- and high-dose only in females. There is no qualitative and/or quantitative evidence of increased susceptibility to reproductive effects of polyxylenol tetrasulfide following pre/postnatal exposure in this study.

A developmental toxicity study in rabbits was also conducted but was found to be unacceptable because significant maternal toxicity (including dam deaths) was evident in all study groups including the control group. It was determined that the carrier used in this study, tricaprylin, was likely the contributing factor to these effects.

An acceptable developmental toxicity study for polyxylenol tetrasulfide will be required in order to confirm the lack of developmental effects from exposure to this chemical.

3. MUTAGENICITY

The submitted studies on mutagenicity were found to be acceptable. There was no concern for mutagenicity resulting from exposure to polyxylenol tetrasulfide.

4. CARCINOGENICITY

No data is available on the potential carcinogenicity of polyxylenol tetrasulfide. However, the negative results in the mutagenicity battery do not indicate a concern for carcinogenicity.

B. TOXICOLOGICAL ENDPOINTS

Toxicological endpoint selections, and appropriate margins of exposure (MOEs) for use as appropriate in occupational exposure risk assessments, are summarized in Table 1 below:

Table 1: Toxicity Endpoints Selected for Assessing Occupational Risk for Polyxylenol Tetrasulfide

Exposure Scenario	Dose Used in Risk Assessment	Level of Concern for Risk Assessment	Study and Toxicological Effects
Short-Term Dermal	Dermal LOAEL = 125 mg/kg/day	**Occupational LOC for MOE =** 300	Reproduction/developmental screening toxicity Maternal NOAEL = Not established Maternal LOAEL = 125 mg/kg/day based on based on short-term hematological effects.
Intermediate- and Long-Term Dermal	Dermal LOAEL = 125 mg/kg/day	**Occupational LOC for MOE =** 1000	Reproduction/developmental screening toxicity Maternal NOAEL = Not established Maternal LOAEL = 125 mg/kg/day based on based on short-term hematological effects.
Short-, Intermediate-, and Long-Term Inhalation	Insufficient data available		
Cancer	No cancer data available for polyxylenol tetrasulfide		

C. FQPA CONSIDERATIONS

Polyxylenol tetrasulfide is not currently proposed for any residential or food uses. Since the only proposed uses are in the commercial and industrial settings an FQPA hazard analysis is not required at this time.

III. HUMAN HEALTH RISK ASSESSMENT

Exposure pathways resulting from the use of polyxylenol tetrasulfide are occupational. There are no residential uses.

A. OCCUPATIONAL RISK ASSESSMENT

Polyxylenol tetrasulfide is intended for use as a pressure treatment for wood products to be used in commercial and industrial settings including as railroad ties, utility poles and aquatic pilings. Based on the uses found on the label, exposure assessments were performed for representative scenarios which were considered to have the potential for the most exposure. These scenarios included:

- occupational workers (treatment assistant, treatment operator) using the product to pressure-treat wood; and
- Post-application exposure to workers (tram setter, stacker operator, loader operator, supervisor, test borer, and tallyman) handling pressure-treated wood.

Handler Exposure and Risk Estimates

No chemical-specific data were available with which to assess the potential exposure to pesticide handlers. Using surrogate unit exposure data, application rates from labels, and EPA estimates of daily amount handled, exposures to handlers were assessed.

Dermal exposures for pressure treatment uses are derived from information in the exposure study by the American Chemistry Council (2002) entitled "*Assessment of Potential Inhalation and Dermal Exposure Associated with Pressure Treatment of Wood with Arsenical Wood Products*" (ACC, 2002). In this study, a treatment solution of CCA was approximately 0.5 percent. The CCA study is the best pressure treatment data available (water based solution) to estimate exposure to polyxylenol tetrasulfide.

Polyxylenol tetrasulfide dermal and inhalation handler exposures and risks can be estimated using the CCA unit exposures. The CCA handler job functions of treating operator (TO) and treating assistant (TA) are used as a surrogate for the pressure treatment operators at polyxylenol tetrasulfide treatment facilities. The normalized unit exposures (µg As/ ppm treatment solution) are extrapolated to the concentration of polyxylenol tetrasulfide in Verigard Blend D (53.9%).

Polyxylenol tetrasulfide is a polymeric chemical. As such, the chemical was forwarded to the OPPT Structure Activity Team (SAT) to consider whether or not the chemical would be subject to the polymer exemption and, if not, what could be determined about dermal absorption. Largely based upon its molecular weight and molecular configuration the SAT review indicated that dermal absorption of PXTS is likely to be poor to nil. Based on this information the Agency refined the risk assessment by using an assumption of a 1 % dermal absorption factor for polyxylenol tetrasulfide.

The calculated dermal MOEs for TO and TA are 800 and 6800, respectively. The Agency also

calculated the MOE (MOE=6000) for TO at U.S. sites. All of these MOEs are above the short-term target MOE (300). All but one of these MOEs is above the intermediate/long-term target MOE (1000).

Since polyxylenol tetrasulfide is a solid at room temperature it must be heated in order for it to be used to treat wood. Given the lack of information characterizing how this material behaves when it is heated during the pressure treatment process and the potential implications for inhalation exposures, no toxicological endpoints have been identified and a quantitative risk assessment has not been conducted for this route of exposure. The available database for polyxylenol tetrasulfide is not sufficient to determine whether exposure is likely to occur via this route once heated during treatment or the nature of such an exposure (i.e. aerosol and/or vapor). In the absence of the necessary inhalation data, the Agency will sometimes use an oral endpoint and additional uncertainty factors to estimate potential inhalation (aerosol) risks. Using the oral endpoints for a route-to-route extrapolation, the inhalation risk estimates are not of concern do not exceed the Agency's level of concern (MOEs > 1000). However, based on the uncertainties noted above (i.e. does polyxylenol tetrasulfide form a vapor when heated at treatment temperatures?), the Agency is requiring data on the chemistry of polyxylenol tetrasulfide when heated as a condition of this registration.

Post-application Exposure and Risk Estimates

Polyxylenol tetrasulfide dermal and inhalation post-application exposures and risks can be estimated using the CCA unit exposures. The post-application job functions include: tram setter (TS); stacker operator (SO); loader operator (LO); supervisor (S); test borer (TB); and the tallyman (TM). The exposures for these job functions have been combined into one data set to represent post-application activities because for most activities the sample size is small ($5 \leq n \leq 15$).

The normalized unit exposures (μg As/ppm treatment solution) are extrapolated to the concentration of polyxylenol tetrasulfide in Verigard Blend D (53.9%). The calculated dermal MOEs for occupational post-application exposure associated with pressure treatment are 2200 and 3300, which are above both the short- and long-term target MOEs (300 and 1,000, respectively).

Uncertainties

- **CCA Study**: CCA exposure data were used for lack of -specific exposure data. Limitations and uncertainties associated with the use of these data include:
    - The assumption was made that exposure patterns for workers at pressure treatment facilities using CCA would be similar to, and therefore could be used as surrogate data for, workers that treat wood with polyxylenol tetrasulfide. Additionally, the CCA data were normalized by the treatment solution concentration and the polyxylenol tetrasulfide exposures were adjusted accordingly (i.e., extrapolated from 0.5 percent CCA up to 53.9

percent polyxylenol tetrasulfide).

- For post-application scenarios, it was assumed that exposures for workers handling polyxylenol tetrasulfide -treated wood would be similar to those from CCA-treated wood. However, due to the lack of real data for polyxylenol tetrasulfide -treated wood, it is not possible to verify this assumption.
- Polyxylenol tetrasulfide Blend D is a solid at room temperature and must be heated 68 °C to 122 °C before applying the product. For lack of better data, it is assumed that heating the product does not affect the applicability of the CCA data as surrogate data.
- Polyxylenol tetrasulfide Blend D is applied at full strength, while CCA is applied at a diluted concentration. For lack of better data, it is assumed that the lack of a mixing procedure in the use of polyxylenol tetrasulfide does not affect the applicability of the CCA data as surrogate data. However, the linear extrapolation of CCA exposure data at 0.5% to the PXTS solution of 53.9% is believed to be an overestimate of exposure.
- CCA is a water-based solution whereas polyxylenol tetrasulfide appears to be more oil-based. Thus, use of CCA data may not be appropriate for polyxylenol tetrasulfide; however, again it was assumed that worker exposures would be similar.
- There is a high degree of variability in the CCA dermal and inhalation Unit Exposures (UEs). This high variability increases the uncertainty of the polyxylenol tetrasulfide assessment. For example, the average (mean) dermal UE for US-post-application job functions was determined to be 0.49 ug As/ppm, but this value has a standard deviation of $\pm$ 0.51 ug As/ppm. This value is as large as the mean and indicates large variability in the mean value, thus, increasing the assessment's uncertainty.
- The CCA study is based on 3-6 treatment cycles per work day at two sites and one treatment cycle at the third site. Polyxylenol tetrasulfide treatment cycles are expected to be less frequent (1-2 cycles per work day). Therefore, exposures derived using the CCA data are expected to be measurably higher than are expected for polyxylenol tetrasulfide.

E. CUMULATIVE RISK

A cumulative risk assessment was not done for polyxylenol tetrasulfide, as the Agency has not made a common mechanism of toxicity finding with any other chemical substances, and polyxylenol tetrasulfide does not appear to produce a toxic metabolite produced by other substances.

F. INCIDENTS

Polyxylenol tetrasulfide is a new active ingredient with no reported incidents.

IV. ENVIRONMENTAL RISK ASSESSMENT

Ecotoxicity testing was difficult given the low solubility of polyxylenol tetrasulfide and its' tendency to bind to glassware. Agreement was made early in the registration process to utilize solvents to achieve a maximum dosage level of 10X the solubility (maximum dosage = 125 ppb). Therefore, tests at dosage levels greater than 125 ppb were not required. The most sensitive organisms tested were marine mollusks (see below) and the diatoms (*Skeletonema costatum*) and (*Navicula pelliculosa*). All other organisms tested in acute toxicity tests (freshwater fish, marine fish, Daphnia magna, Mysid shrimp, green algae, blue-green cyanobacteria, rice seedling emergence, and a floating freshwater aquatic macrophyte) have acute LC50/EC50 and NOAEC values > 125 ug/l (ppb).

Acute toxicity test results for the most sensitive aquatic species are:

Eastern Oyster -	EC50 = 64.0 ug/l, NOAEC = 31.0 ug/l (Supplemental/Invalid*)
Freshwater diatom -	EC50 = 48.0 ug/l, NOAEC = 31.0 ug/l
Marine diatom -	EC50 = >125.0 ug/l, NOAEC = 63.0 ug/l

Acute sediment toxicity tests were requested and submitted by the registrant and found to be invalid, but upgradeable to supplemental pending receipt of additional information. Reported results were:

850.1735 - Whole sediment acute toxicity invertebrate freshwater:

10-day EC50 = > 100 mg/kg dry sediment
NOEC = > 100 mg/kg dry sediment
LOEC = > 100 mg/kg dry sediment

850.1740 - Whole sediment acute toxicity invertebrates marine:

10-day EC50 = 42 (95 % C.L.: 25 – 30) mg/kg dry sediment
NOEC = 25 mg/kg dry sediment
LOEC = 50 mg/kg dry sediment

Given the fate of polyxylenol tetrasulfide in the environment, a percentage is expected to partition to sediment where it is tightly bound. Repeated exposures may result in increased concentrations in sediments over time, resulting in potential for chronic impacts on aquatic organisms. Chronic toxicity tests were requested of the registrant; however, after consideration of the difficulties with keeping polyxylenol tetrasulfide in solution for long time periods, as required in chronic toxicity tests, the Agency has decided to hold the studies in reserve at this time.

A. ENVIRONMENTAL FATE ASSESSMENT

Presently, limited fate data are available. These data indicate that polyxylenol tetrasulfide is

stable in water and does not readily hydrolyze. Polyxylenol tetrasulfide leaches at low levels out of wood under laboratory conditions.

B. ECOLOGICAL EFFECTS AND RISK

Terrestrial

Terrestrial EECs were not calculated since it is anticipated that exposures and risks for terrestrial organisms (birds, mammals, and plants) to polyxylenol tetrasulfide during in-service use should be minimal.

Terrestrial RQs were not calculated since the Agency believes that exposures and risks for terrestrial organisms (birds, mammals, and plants) to polyxylenol tetrasulfide during in-service use are expected to be minimal.

Aquatic

To estimate potential exposure in the aquatic environment the Agency initially implemented an approach using a surrogate dock and various pond sizes. This approach yielded aquatic EECs for both freshwater and saltwater. However, because of the uncertainties with using such an approach for a chemical with limited solubility, such as polyxylenol tetrasulfide, the Agency has decided to use the maximum level of solubility as the aquatic EEC for polyxylenol tetrasulfide: i.e., 12.5 ppb.

- None of the LOCs are exceeded for aquatic organisms found typically in the water column and, therefore, polyxylenol tetrasulfide is not expected to adversely affect such organisms. Also, for organisms such as mollusks, a dose-response was observed in the available mollusk study (MRID 462115-01). However, because of numerous issues with the study the Agency has decided not to use the study in a quantitative manner. Therefore, the Agency has utilized the mysid shrimp LC50 of > 125 ppb (MRID 460626-28) for mollusk species. Use of the 12.5 ppb EEC results in a value below the LOCs established for non-endangered and endangered aquatic species. Therefore, polyxylenol tetrasulfide is not expected to adversely affect such species;

- For diatoms, which have an established EC50 or NOAEC value (e.g., freshwater diatom EC50 = 48 ppb), use of the 12.5 ppb EEC results in values below the plant LOC of 1.0 established for non-endangered and endangered plants species. Therefore, polyxylenol tetrasulfide is not expected to adversely affect such plant species.

C. ENDANGERED SPECIES CONCERNS

The Agency concludes that, based on the available information and data, a Not Likely to Adversely Affect (NLAA) determination can be made at this time for terrestrial and aquatic organisms. However, with the submission of additional data a more refined assessment can be made.

D. UNCERTAINTIES

The following factors/issues affect the ecological risk characterization resulting in a moderate to high degree of uncertainty in the assessment.

- **Leaching from wood and solubility**: The leaching data from the study (MRID 460626-25, -26) submitted by the registrant may overestimate the amount of polyxylenol tetrasulfide, metabolites, and/or degradates, which leach out of wood because the conditions under which the study was conducted may not be similar to those under field environmental conditions. The type, age and wood treatment process may affect leaching of the chemical from wood. Also, it is noted that according to the report an organic compound leaches out along with polyxylenol tetrasulfide, which increases the solubility of this compound in water. This report does not state what this organic compound is. Conversely, during typical treatment of wood, treated wood may not be thoroughly impregnated with polyxylenol tetrasulfide.

- **Ecotoxicity data**: Many of the available ecotoxicity tests are maximum limit tests, which only tested PXTS at a level 10x the solubility level. A risk assessment that utilized more defined LC50s/EC50s would be advantageous, but in this case was not possible. Additionally, there were numerous issues with the mollusk study, which resulted in the Agency not utilizing this study at this time.

- **Limited fate data**: Presently, limited fate data are available. More fate data performed under actual use conditions would enable the Agency to refine its assessment.

V. RISK MANAGEMENT DECISION

Available data provide adequate information to support the conditional registration of polyxylenol tetrasulfide technical and end-use products for use as a pressurized wood treatment for wood products to be used in industrial/commercial settings.

Although one of the occupational MOEs does not exceed the target MOE of 1000, the Agency believes that there are significant uncertainties in the risk assessment which lead it to believe that the actual exposures expected from the use of polyxylenol tetrasulfide will not exceed the Agency's level of concern and allows for adequate protection of workers. These uncertainties include the limitations associated with the use of CCA data to predict exposures to polyxylenol tetrasulfide given the differences between the chemicals.

VI. LABELING RESTRICTIONS

No labeling restrictions are necessary at this time.

VII. CONFIRMATORY DATA REQUIREMENTS

Additional studies are needed to be able to refine the risk assessment. As indicated below, some studies are required as a condition of registration while others are held in reserve.

A. The following studies are **required** as a condition of registration:

- **Chemistry Data at Treatment Temperatures**: Data are required to clarify inhalation exposures to workers when heating polyxylenol tetrasulfide in wood treatment plants. The registrant has committed to conducting the study in order to provide data on vapor pressure and particle size of the heated test material in order to determine whether there is potential for significant inhalation exposure.

- **21-Day Dermal Toxicity Data**: In order to more accurately determine the dermal absorption/hazard of PXTS and to better refine the final dermal MOES, which are based on 1 % dermal absorption, a rodent 21-day dermal toxicity study is required (870.3250).

- **Prenatal Developmental Toxicity Study in rodents [870.3700a]:** No acceptable developmental study is available for polyxylenol tetrasulfide.

- **Oyster study [72-3(b), 850.1055]**: Considering the number of issues associated with the mollusk shell-growth study, we recommend that another estuarine/marine invertebrate study be performed, but one that uses oyster embryo-larvae, where mortality and/or failure to develop complete shells are measured. In such a study, either: (a) a maximum limit test could be performed (e.g., at levels of 125 ppb); or (b) testing with the form that will be present in water (when polyxylenol tetrasulfide is bound to an organic resin, as shown in the wood leaching study) be performed. However, we recognize that it may not be feasible to obtain enough of the latter compound to perform such a study; further discussion with the registrant on this subject is warranted.

- **Soil metabolism, anaerobic (162-2)**: As agreed to in the 9/14/05 teleconference between Agency scientists and polyxylenol tetrasulfide representatives concerning use of radio-labeled surrogate in the anaerobic soil metabolism study: (1) Agency staff agreed to use of ring-labeled para-cresol oligomer as a surrogate test substance when radio-labeled test material is required in tier two testing, specifically for anaerobic and aerobic soil metabolism studies; (2) the radio-labeled surrogate will be mixed into non-labeled polyxylenol tetrasulfide, and the combined mixture will be the test substance; and (3) the registrant will provide a 6-month interim report on the soil metabolism studies to the Agency, as this study may run up to 12-months before a final report can be issued.

Reserved Studies

The following studies are reserved, pending submission and review of the above required studies and information and may be required at a later date.

- Human Exposure Data – Worker Exposures - (application - 875.1100, 875.1200, 875.1300, 875.1400, 875.1500, 875.1600, and 875.1700; post-application - 875.2400, 875.2500, 875.2600, 875.2700, 875.2800, and 875.2900)
- Human Exposure Data - Dislodgeable Residue - (Surface Wipe Sampling) [EP; 875.2300, 875.2900; also, refer to CPSC (2003a), CPSC (2003b), CPSC (2003c), CPSC (2003d), CPSC (2003e), RTI International (2003).
- Chironomid sediment toxicity test - 850.1790
- Fish Early Life Stage- 850.1400
- *Daphnia* chronic toxicity (or) 850.1350 - *Mysid* chronic toxicity - 850.1300
- Oyster BCF - 850.1710
- Honeybee acute contact LD50 - 850.3020
- Aquatic field dissipation study [164-2]

RECOMMENDATION

Available data provide adequate information to support the registration of polyxylenol tetrasulfide technical and end-use products for use as a treatment for wood products to be used in industrial/commercial settings.

I recommend that you concur with the conditional registrations of this new chemical antimicrobial under Section 3(c)(7) of the Act.

CONCUR

12/20/05
DATE

DO NOT CONCUR

DATE