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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

12/22/1998

MEMORANDUM

Subject: D249787
ACQ 2102, Product No. 10465-GO

D249764
ACQ 2101, Product No. 10465-UN

From: Wallace Powell, Biologist
Efficacy and Science Support Branch
Antimicrobials Division (7510W)

Thru: Michele E. Wingfield, Chief
Efficacy and Science Support Branch
Antimicrobials Division (7510W)

To: Adam Heyward, Product Manager, Team 34
Portia Jenkins, Team Reviewer, Team 34
Regulatory Management Branch II
Antimicrobials Division (7510W)

BACKGROUND.

In a 5/05/98 letter to the applicant, Chemical Specialties Inc., the Agency waived acute dermal toxicity, acute inhalation toxicity, primary eye irritation, primary dermal irritation, and dermal sensitization data, for the wood preservative products ACQ 2102 (EPA Product No. 10465-GO) and ACQ 2101 (EPA Product No. 10465-UN). The Agency denied the applicant's acute oral toxicity waiver request for these products.

The latest submission from the applicant contains two acute oral toxicity studies – MRID No. 446513-01 conducted on ACQ 2101, and MRID No. 446514-01 conducted on ACQ 2102. The studies were reviewed for Efficacy and Science Support Branch (ESSB) by Oak Ridge National Laboratory. The reviews are attached to this memorandum (and are included in the same electronic folder, as separate files).

RECOMMENDATION

§81-1, Acute Oral Toxicity: Both submitted studies indicate Toxicity Category III (i.e., 500 mg/kg < LD_{50} ≤ 5000 mg/kg) and are acceptable.

§81-3, Acute Inhalation Toxicity:

Although the Agency waived acute inhalation toxicity data for the two subject products, it assigned Toxicity Category I to this acute effect in the absence of data to the contrary. Because of the corrosiveness of the products, adequate label hazard statements are necessary. The products (or one of their various dilutions) might result in death if inhaled.

The subject products are labeled for two uses: vacuum-pressure wood treatment and spray treatment. The pressure treatment occurs inside an enclosed cylinder. According to Jim Saur, the applicant's Vice President for Regulatory Affairs (12/22/98 telephone conversation between him and this reviewer), the spray treatment occurs inside an enclosed booth located on a drip pad. The spray nozzles are stationary and emit a coarse, low pressure spray. A negative pressure is created inside the enclosed booth, in order to further contain the material. The booth is equipped with scrubbers. The scrubbers may cause displacement of some material into the air inside the booth, which is also equipped with exhaust. Mr. Saur also said that if workers are on the drip pad while the spray application is occurring, they are not required to wear respirators – e.g., under OSHA regulations.

The inhalation Category I rating has been reconsidered. It appears that the Category I labeling would require workers to wear respirators in a well-established type of industrial treatment situation in which they are not currently required to do so. On the one hand, we wonder if the spray booth setup in the above paragraph describes an ideal that some treatment plants might fall short of. On the other hand, however, we don't want to introduce a requirement where it appears that there is none, in a situation that is already regulated by another authority, a situation in which other registrants' corrosive products are also commonly used. Moreover, the labels for the subject products appear to contain adequate precautions (with one exception – see below), which bear resemblance to acute inhalation Category I or II labeling. The labels contain the statement, "May be fatal if ... inhaled," as well as instructions for persons who enter pressure-treatment cylinders to wear high-efficiency respirators. Acute inhalation Category II is being assigned, for the record.

However, the proposed label should be revised to more explicitly require respirator use for persons who enter the spray treatment booth. (See PRODUCT LABELING section below.)

The acute toxicity regulatory profile, which is the same for both products, is summarized in the table below.

Acute Effect	MRID No.	Toxicity Category Assigned
Acute Oral Toxicity	446513-01 (for ACQ 2101) 446514-01 (for ACQ 2102)	III
Acute Dermal Toxicity	waived previously	IV
Acute Inhalation Toxicity	waived previously	II
Primary Eye Irritation	waived previously	I
Primary Dermal Irritation	waived previously*	I
Dermal Sensitization	waived previously	Sensitizing

* Previous review indicated 'cited' rather than 'waived'. It appears that what was 'cited' was a product, not a study.

PRODUCT LABELING

Based on the above acute toxicity regulatory profile, the required precautionary and practical treatment label statements, in accordance with the *Label Review Manual* (December 1996 edition) are as follows. They are the same for both the subject products.

Signal Word: DANGER

Precautionary statements to appear under the heading HAZARDS TO HUMANS AND DOMESTIC ANIMALS:

> DANGER. Corrosive. Causes skin burns and irreversible eye damage. May be fatal if inhaled. Harmful if swallowed. Do not get in eyes, on skin, or on clothing. Wear protective goggles or face shield, protective clothing, and rubber gloves *[or specify a type of chemical-resistant gloves]*. Do not breathe vapors. Wear a mask or pesticide respirator approved by the National Institute for Occupational Safety and Health. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

Accordingly, the HAZARDS TO HUMANS AND DOMESTIC ANIMALS paragraph should be revised as follows:

- Delete the phrase "absorbed through skin" from the statement, "May be fatal if ... absorbed through skin."
- Add the statement, "Do not breathe vapors."
- The statement, "Individuals who enter pressure treatment cylinders and other related equipment contaminated with wood treatment solution...," needs to be revised to explicitly

include spray-treatment booths/compartments. Arguably, the term "other related equipment" is not explicit enough.

The STATEMENT OF PRACTICAL TREATMENT section of the submitted labels (EPA Received date 09/14/98) is fully in accordance with the *Label Review Manual* and is acceptable.

DATA EVALUATION REPORT

COPPER AMMONIUM CARBONATE
(PRODUCT ACQ 2102)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT (81-1)

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. 241

Primary Reviewer: Susan Chang, M.S.	Signature: Date:	S S Chang 10-12-98
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.	Signature: Date:	H.T Borges 10-12-98
Robert H. Ross, M.S., Group Leader	Signature: Date:	Robert H. Ross 10-12-98
Quality Assurance: LeeAnn Wilson, M.A.	Signature: Date:	L. A. Wilson 10-12-98

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

EPA Reviewer: Wallace Powell, Ph.D. Wallace D Powell, Date 12-22-98
EPA Work Assignment Manager: Peter Thompson, Ph.D. _____, Date _____

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS 870.1100 [§81-1]

DP BARCODE: D249787 SUBMISSION CODE: S549154
P.C. CODE: 022703 TOX. CHEM. NO.:

TEST MATERIAL (PURITY): Product ACQ 2102 (purity not reported)

SYNONYMS: None reported

CITATION: Allen, D.J. (1998) Product ACQ 2102: Acute oral toxicity test in the rat. Safepharm Laboratories Limited, P.O. Box 45, DERBY, DE1 2BT, UK. Project No. 577/037, September 3, 1998. MRID 44651401. Unpublished.

SPONSOR: Chemical Specialties Inc., One Woodlawn Green, Suite 250, Charlotte, NC 28217

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44651401) groups of five male and five female fasted young adult Sprague-Dawley rats were given a single oral 1000, 1414, or 2000 mg/kg dose of Product ACQ 2102 (purity not reproted, Batch no. 98-0408B) and observed for 14 days.

Hunched posture, lethargy, and/or piloerection were noted on all rats. Ataxia, decreased respiratory rates, and/or labored breathing were noted in the mid- and high dose groups. Pallor of the extremities, gasping, noisy respiration, loss of righting reflex, increased salivation and/or splayed gait were noted in females from the mid-dose group. The surviving rats recovered by day 9 or earlier. All surviving rats had gained weight throughout the study. Hemorrhagic lungs, dark liver/kidney, blue contents in stomach, sloughing and stained blue gastric mucosa/stomach, and/or hemorrhagic intestines were noted among the decedents. The surviving female in the high-dose group had an ulcerated stomach. The other surviving rats had no abnormalities.

Oral LD_{50} Males < 2000 mg/kg and > 1414 mg/kg
Females = 1189 mg/kg (95% C.L. 652-2167 mg/kg)
Combined = 1523 mg/kg (95% C.L. 1284-1808 mg/kg)

Product ACQ 2102 is in TOXICITY CATEGORY III based on the LD_{50} in females.

This acute oral study is classified acceptable (guideline). This study does satisfy the guideline requirement for an acute oral study (81-1) in the rat.

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COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Product ACQ 2102

   Description: dark blue liquid
   Lot/Batch #: 98-0408B
   Purity: not reported
   CAS #: not reported

2. Vehicle and/or positive control

   None

3. Test animals

   Species: rat
   Strain: Sprague-Dawley CD(Crl:CD®BR)
   Age and/or weight at dosing: 8-12 weeks; Males: 216-268 g, females: 201-244 g
   Source: Charles River (UK) LTD, Margate, Kent
   Acclimation period: ≥5 days
   Diet: Rat and Mouse Expanded Diet No. 1 (Special Diets Services Limited), *ad libitum*
   Water: tap water, *ad libitum*
   Housing: groups of up to five in solid-floor polypropylene cages furnished with woodflakes
   Environmental conditions:
   Temperature: 19-22°C
   Humidity: 50-67%
   Air changes: 15/hour
   Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

   Start: May 27, 1998; end: July 2, 1998

2. Animal assignment and treatment

   Following an overnight fast, five rats/sex/dose were given a single 1000, 1414, or 2000 mg/kg dose of the test material by gavage. The animals were observed for

mortality and clinical signs of toxicity 1/2, 1, 2, and 4 hours after dosing and once daily for up to 14 days. They were weighed on study days 0, 7, or 14 and at death. Survivors were sacrificed and all animals were necropsied.

3. Statistics

Calculation of the male oral LD_{50} was by the method of Thompson WR, Bact. Reviews, 11, 115-145 (1947).

II. RESULTS AND DISCUSSION

A. Mortality is given in Table 1.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
1000	0/5	2/5	2/10
1414	0/5	3/5	3/10
2000	5/5	4/5	9/10

Data taken from Table 2, p. 19, MRID 44651401.

One female in the low-dose group, three females each in the high- and mid-dose groups, and one male in the high-dose group died within four hours of test material administration. One female in the low-dose group and four males and one female in the high-dose group died within one day of test material administration.

The oral LD_{50} for males is < 2000 mg/kg and > 1414 mg/kg
Females is 1189 mg/kg (95% C.L. 652-2167 mg/kg)
Combined is 1523 mg/kg (95% C.L. 1284-1808 mg/kg)
Product ACQ 2102 is in TOXICITY CATEGORY III based on the LD_{50} in females.

B. CLINICAL OBSERVATIONS

Hunched posture, lethargy, and/or piloerection were noted in all rats. Ataxia, decreased respiratory rate, and/or labored breathing were noted in the mid- and high dose groups. Pallor of the extremities, gasping, noisy respiration, loss of righting reflex, increased salivation and/or splayed gait were noted in the females in the mid-dose group. The surviving rats recovered by day 9 or earlier.

C. BODY WEIGHT

All surviving rats gained weight throughout the study.

D. NECROPSY

Hemorrhagic lungs, dark liver/kidney, blue contents in stomach, sloughing and stained blue gastric mucosa/stomach, and/or hemorrhagic intestines were noted among the decedents. The surviving female in the high-dose group had an ulcerated stomach. The other surviving rats had no abnormalities.

E. DEFICIENCIES

Purity of the test material was not reported. This would not affect the study results.

DATA EVALUATION REPORT

COPPER AMMONIUM CARBONATE
(PRODUCT ACQ 2101)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT (81-1)

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. 240

Primary Reviewer: Susan Chang, M.S.	Signature: Date:	S S Chang 10-12-98
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.	Signature: Date:	H T Borges 10-12-98
Robert H. Ross, M.S., Group Leader	Signature: Date:	Robert H. Ross 10-12-98
Quality Assurance: LeeAnn Wilson, M.A.	Signature: Date:	L. A. Wilson 10-12-98

Disclaimer

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

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EPA Reviewer: Wallace Powell, ~~Ph.D~~. _____, Date 12-22-98
EPA Work Assignment Manager: Peter Thompson, Ph.D _____, Date _____

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS 870.1100 [§81-1]

DP BARCODE: D249764
P.C. CODE: 022703

SUBMISSION CODE: S549096
TOX. CHEM. NO.:

TEST MATERIAL (PURITY): Product ACQ 2101 (purity not reported)

SYNONYMS: None reported

CITATION: Allen, D.J. (1998) Product ACQ 2101: Acute oral toxicity test in the rat. Safepharm Laboratories Limited, P.O. Box 45, DERBY, DE1 2BT, UK. Project No. 577/036, September 3, 1998. MRID 44651301. Unpublished.

SPONSOR: Chemical Specialties Inc., One Woodlawn Green, Suite 250, Charlotte, NC 28217

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44651301) groups of five male and five female fasted young adult Sprague-Dawley rats were given a single oral 500 (females only), 1000, 1414, or 2000 mg/kg dose of Product ACQ 2101 (purity not reported, Batch no. 98-0408A) and observed for 14 days.

Hunched postures and decreased respiration rates were noted in all rats. Lethargy, labored/noisy respiration, piloerection, ptosis, ataxia, staining around the snout/eyes, tiptoe gait, dehydration, emaciation, pallor extremity, and/or prostration were noted on one or more rats. The surviving rats recovered by day 11 or earlier. All surviving rats gained weight throughout the study with the exception of one female in the low-dose group that lost weight during the first week. Hemorrhagic lungs, dark/patchy pallor liver, dark/blue stained kidneys, pale spleens, blue contents in stomach, sloughing and stained blue gastric mucosa, and/or hemorrhagic/blue stained intestines were noted among the decedents. Some surviving rats had sloughing/thickening/white foci present in stomach and/or thickening of the gastric mucosa. Some surviving rats in the 500 and 1414 mg/kg groups had no abnormalities.

Oral LD_{50} Males is 1542 mg/kg (95% C.L. 1290-1844 mg/kg)
Females is 595 mg/kg (95% C.L. 386-917 mg/kg)
Combined is 1297 mg/kg (95% C.L. 924-1821 mg/kg)
Product ACQ 2101 is in TOXICITY CATEGORY III based on the LD_{50}.

This acute oral study is classified acceptable (guideline). This study does satisfy the guideline requirement for an acute oral study (81-1) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Product ACQ 2101

   Description: dark blue liquid
   Lot/Batch #: 98-0408A
   Purity: not reported
   CAS #: not reported

2. Vehicle and/or positive control

   None

3. Test animals

   Species: rat
   Strain: Sprague-Dawley CD(Crl:CD®BR)
   Age and/or weight at dosing: 8-12 weeks; Males: 210-268 g, females: 200-228 g
   Source: Charles River (UK) LTD, Margate, Kent
   Acclimation period: ≥5 days
   Diet: Rat and Mouse Expanded Diet No. 1 (Special Diets Services Limited), *ad libitum*
   Water: tap water, *ad libitum*
   Housing: groups of up to five in solid-floor polypropylene cages furnished with woodflakes
   Environmental conditions:
   Temperature: 19-23 °C
   Humidity: 48-67%
   Air changes: 15/hour
   Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

   Start: May 27, 1998; end: July 28, 1998

2. Animal assignment and treatment

Following an overnight fast, five rats/sex/dose were given a single 500 (females only), 1000, 1414, or 2000 mg/kg dose of the test material by gavage. The animals were observed for mortality and clinical signs of toxicity ½, 1, 2, and 4 hours after dosing and once daily for up to 14 days. They were weighed on study days 0, 7, or 14 and at death. Survivors were sacrificed and all animals were necropsied.

3. Statistics

Calculation of the male oral LD_{50} was by the method of Thompson WR, Bact. Reviews, 11, 115-145 (1947).

II. RESULTS AND DISCUSSION

A. Mortality is given in Table 1.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
500	-	1/5	-
1000	1/5	5/5	6/10
1414	1/5	2/5	3/10
2000	5/5	5/5	10/10

Data taken from Table 2, p. 20, MRID 44651301.

Three females in the 1000 mg/kg group and three male and two female rats in the high-dose groups died within four hours of test material administration. One female in the low-dose group, one male and two females rats in the 1000 mg/kg group, one male and two female rats in the 1414 mg/kg group, and one male and three female rats in the high-dose group died within one day of test material administration. One male in the high-dose group died within two days of treatment.

The oral LD_{50} forMales is 1542 mg/kg (95% C.L. 1290-1844 mg/kg)
Females is 595 mg/kg (95% C.L. 386-917 mg/kg)
Combined is 1297 mg/kg (95% C.L. 924-1821 mg/kg)
Product ACQ 2101 is in TOXICITY CATEGORY III based on the LD_{50}.

B. CLINICAL OBSERVATIONS

Hunched postures and decreased respiration rates were noted in all rats. Lethargy, labored/noisy respiration, piloerection, ptosis, ataxia, staining around the snout/eyes, tiptoe gait, dehydration, emaciation, pallor extremities, and/or

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prostration were noted on one or more rats. The surviving rats recovered by day 11 or earlier.

C. BODY WEIGHT

All surviving rats gained weight throughout the study with the exception of one female in the low-dose group that lost weight during the first week.

D. NECROPSY

Hemorrhagic lungs, dark/patchy liver, dark/blue stained kidneys, pale spleens, blue contents in stomach, sloughing and stained blue gastric mucosa, and/or hemorrhagic/blue stained intestines were noted among the decedents. Some surviving rats had sloughing/thickening/white foci present in stomach and/or thickening of the gastric mucosa. Some surviving rats in the 500 and 1414 mg/kg groups had no abnormalities.

E. DEFICIENCIES

Purity of the test material was not reported. This would not affect the study results.