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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

ENVIRONMENTAL CHEMISTRY SECTION  
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JUN 16 1995

MEMORANDUM

SUBJECT: DC-5772® (Anti-Microbial Agent) Method Review Summary -  
Report No. ECM 0059W1

FROM: Aubry Dupuy, Jr., Section Chief *Aubry E. Dupuy, Jr.*  
BEAD/ACB/Environmental Chemistry Section

TO: Anthony F. Maciorowski, Branch Chief  
EFED/Ecological Effects Branch (7507C)

THRU: Donald A. Marlow, Branch Chief *DM*  
BEAD/Analytical Chemistry Branch (7503W)

The EFED/Environmental Fate and Effects Division has requested an Environmental Chemistry Method Review Summary (ECME) on DC-5772® in aqueous buffered solutions, using the ABC Laboratories/Dow Corning Corporation, Health & Environmental Science Division analytical method, "Hydrolysis of DC-5772 as a Function of pH".

The attached method evaluation report includes three parts:

Part I: Method Review Summary

In this section a description of the method is presented.

Part II: Method Problems

In this section the problems associated with the analytical method and results are discussed. The analytical method together with recoveries of the analyte and the relative standard deviation (RSD) for each spiking level are reviewed. Any inherent problems are introduced.

Part III: Conclusion

In this section the conclusion of the method review is presented.

If you have any questions concerning this report, please contact Christian Byrne at (601) 688-3213 or me at (601) 688-3212.

**Comments**

cc: **Danny McDaniel, QA Coordinator**  
**BEAD/ACB/Environmental Chemistry Section**

**Christian Byrne**  
**BEAD/ACB/ECS**

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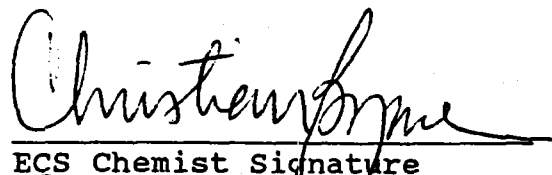
**Environmental Chemistry Method Review Summary  
Number ECM 0059W1**

**DC-5772 in Aqueous Buffered Solutions**

**Environmental Chemistry Section  
Analytical Chemistry Branch  
Biological and Economic Analysis Division**

June 9, 1995

Prepared by: Christian Byrne,

  
ECS Chemist Signature

Reviewed by: Danny McDaniel,

  
ECS/QA Officer Signature

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## PART I

### METHOD REVIEW SUMMARY

#### Method Review

We have completed the review of Environmental Chemistry Method (ECM) on Dow Corning® 5772 Antimicrobial Agent (DC-5772, also known as Dow Corning® Q9-6346 Silane), in buffered reagent water (ECM 0059W1). The ECS Method review was conducted on the ABC Laboratories Final Report #42160 and its associated data files prepared for the Dow Corning Corporation, Health & Environmental Science, Midland, Michigan. The report was based on a study entitled "Hydrolysis of DC-5772 as a Function of pH".

#### Study Summary

The final report of the study entitled "Hydrolysis of DC-5772 as a Function of pH" indicated that a hydrolysis study was conducted with DC-5772 (octadecylaminodimethyltrimethoxysilylpropyl ammonium chloride, the active ingredient) at a theoretical test concentration of 1190 ppm in triplicate aqueous buffer solutions at three different pH values of 5, 7, & 9 held at 25°C. The rate of hydrolysis of the active ingredient was determined by monitoring the decrease of intensity for the methoxy (i.e., CH<sub>3</sub>O-) peak using proton-magnetic resonance spectrometry (<sup>1</sup>H-NMR). The mean hydrolysis half-lives of the active ingredient were 14.6, 7.98, and 3.79 minutes at pH 5, 7, and 9, respectively.

The ABC Laboratories conclude in their final report that the relatively hydrophobic alkoxy silane test material (i.e., DC-5772) underwent hydrolytic conversion to hydrophilic hydrolyzed materials containing silanol (i.e., HO-Si=) groups. The concentration of these hydrolyzed substances was determined by a measure of the total-silicon (Si) in solution by inductively coupled plasma (ICP) emission spectroscopy. Calibration was performed using a spectrometric standard solution of silicon from the National Institute of Standards & Technology (NIST) for the quantitation of total-Si in the test solutions.

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## PART II

### METHOD PROBLEMS

The following are the inherent problems that were determined by the review of the method:

- o In the **SUMMARY Section**, located on page 12 of the **ABC Final Report #42160**, it is stated that "the active ingredient of DC-5772 undergoes a rapid, pH-dependent hydrolysis and is removed from solution in the form of insoluble siloxane resins." In the **TEST PROCEDURE. Composition of Hydrolysis Products**, located on Page 19, it is stated that "a sample was prepared by transferring 6.6 ml of DC-5772 (6.3 g of DC-5772) . . . diluting with 20 ml of reagent water. This sample resulted in a product that "centrifugation was unable to separate the aqueous phase from the precipitate." Therefore, it is apparent from the text that the precipitated hydrolysis products were not true precipitates but were in an emulsion.
- o Attempts to break the resulting emulsion failed and a portion of the emulsion was "evaporated to near dryness using a rotoevaporator . . . The solid precipitate was found to form a gel." <sup>29</sup>Si-NMR analysis was performed on the "the dissolved precipitate"; however, the material never precipitated. Therefore, the description of the material as a precipitate is incorrect.
- o In the **SUMMARY Section**, located on page 12 of the **ABC Final Report #42160**, it is stated that "concentrations of total-Si in the test solutions initially increased as a result of the hydrolytic conversion of the relatively hydrophobic alkoxysilane test material (i.e., DC-5772) to hydrophillic hydrolyzed materials containing silanol (i.e., HO-Si≡) groups." However, in the **TEST PROCEDURE Section. Silicon Concentration**, its is stated that "to measure the total-Si in the aqueous phase of the test samples following the formation of a precipitate, the triplicate samples for all three pH levels were allowed to stand at ambient conditions for 16 hours." Therefore, although the added DC-5772 was undergoing hydrolysis, there was no observable

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precipitate. Therefore, the DC-5772 is most probably present in colloidal suspension.

- o The data provided in the report indicated an inherent problem in the measurement of the concentration of total-silicon (Si) using inductively coupled plasma spectroscopy (ICP) in the test aqueous solution of DC-5772 solution due to the presence of excessive background levels of total-Si in the preparative deionized and reconstituted hard waters. Background concentrations of total-Si in deionized water and reconstituted hard water were approximately 200 and 400 parts-per-billion (ppb), respectively. This is of particular concern due to the low concentrations [i.e. parts-per-billion (ppb) (DC-5772 as Si)] of the toxicity values presented in the data files.
- o The Sample Silicon Concentrations (Table XI), page 36 of the report vary for the three replicate analyses at the respective time internals for a given pH: (the %RSDs range from 7.3 to 57.1%). This indicates that this analytical method for DC-5772 (as Si) is not very precise.
- o The Sample Silicon Concentrations do not compare very favorably with the estimated values as determined by <sup>1</sup>H-NMR at the last <sup>1</sup>H-NMR acquisition time (t ≈ 22-51 min, depending on pH).  
 (If the initial Sample Si Concentration is calculated to have been 1190 ppm (Table XI, page 36) and if one averages the three values for percent of first acquisition (H-NMR) (Tables II-X, pages 27-35) and the three values for Sample Si Concentrations (ICP) (Table XI, page 36), then
 

@ pH 5: Sample Si Concentration by NMR =	123 ppm/
	by ICP = 983 ppm;
pH 7: Sample Si Concentration by NMR =	349 ppm/
	by ICP = 1173 ppm;
pH 9: Sample Si Concentration by NMR =	37 ppm/
	by ICP = 681 ppm).

Therefore, the results of differing analytical methods for the determination of DC-5772 (as Si) are not comparative.



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- o Examination of the linear regression curve for the NIST (#3150-Si) standard would indicate that the actual detection limit for DC-5772 (as Si) would be approximately 100-400 ppb which corresponds with the lower calibration standards used. These detection limits would exceed the lowest observable effect concentrations by an order of magnitude.
- o There are some inconsistencies in the data presented by ABC Laboratories regarding the effect of the sample matrix on the determination of total-Si in deionized water and reconstituted hard water (Table 1) and the determination of method detection limits (40 CFR 136, Appendix B) for 5772-Si in reconstituted water [101 ppb 5772-Si, nominal] and [54 ppb 5772-Si, nominal] (Tables 2 & 3). In the case of the effect of the sample matrix on the determination of total-Si in reconstituted hard water, the data from the linear regression of standard addition (Table 1) would indicate that a minimum detection limit would be approximately 450 ppb. In the case of the the determination of method detection limits (40 CFR 136, Appendix B) for 5772-Si in reconstituted water [101 ppb 5772-Si, nominal] and [54 ppb 5772-Si, nominal], the method detection limit (MDL) from the recovery data of reconstituted hard water samples spiked with 5772-Si at 101 and 54 ppb were 13 and 37 ppb for the respective spiking concentrations. However, the ratio of the emission intensities between the mean spiked samples and the blank (signal-to-noise ratio) does not exceed 1.26. A signal-to-noise factor of 2 is the minimum value for a value to be considered statistically significant. This does not provide significant verification of these MDL for DC-5772 (as Si) values. In addition, the difference in the mean emission intensities of the mean spiked samples is only 6.2%. There appears to be little difference between the two sampling sets and would indicate inadequate accuracy in the method at these concentrations (DC-5772 as Si @54 and 101 ppb). Hence, the data indicates that the MDLs for DC-5772 (as Si) should be greater than 100 ppb.
- o In Procedural Step 7 of 40 CFR 136 Appendix B, there is an optional iterative procedure to verify the reasonableness of the estimates of the MDL and the MDL determinations. In the case of the siloxanols and siloxanes of the DC-5772, the background interferences of the aqueous solutions would suggest that additional work to verify of the MDLs (5772-Si) (13 & 37 ppb) is necessary.

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- o The recommended wavelength and estimated instrumental detection limit for silicon (as SiO<sub>2</sub>) is 58 µg/l (ppb) at 288.158 nm [40 CFR 136 Appendix C. Inductively Coupled Plasma - Atomic Emission Spectrometric Method for Trace Element Analysis of Water and Waste Methods 200.7]. Since silicon is approximately 46.75% by mass of the compound, then the estimated instrumental detection limit for silicon (as Si) would be 27 µg/l (ppb). The calculated range of the MDL for DC-5772 (as Si) was 13-37 ppb. This appears to demonstrate that it will be difficult to determine the presence of the hydrolyzed DC-5772 by ICP emission spectroscopy at the predicted effects concentrations of 4-16 ppb.
- o Overall, the determination of the antimicrobial agent (DC-5772) was in relationship to the atom of silicon present within the active ingredient compound. However, all subsequent discussions of the biological effect levels were in concentrations of DC-5772 (as Si). The low parts-per-billion observable effects concentrations (i.e. 4-16 ppb) were as they relate to the silicon atom mass percent. Converting the concentrations from the mass of measurable silicon atom to the mass of the entire DC-5772 molecule present reveals that the biological effects concentrations are considerable higher. The proposed exposure concentrations was 16-258 ppb DC-5772, the predicted EC<sub>50</sub> was 97 ppb DC-5772, the predicted LOEC was 64 ppb DC-5772, and the predicted NOEC was 32 ppb DC-5772 for rainbow trout. The proposed exposure concentrations was 64-1030 ppb DC-5772, the predicted EC<sub>50</sub> was 515 ppb DC-5772, the predicted LOEC was 258 ppb DC-5772, and the predicted NOEC was 129 ppb DC-5772 for *Daphnia magna*. The estimated minimum detection limits for DC-5772 as calculated by ABC Laboratories would range from 200-590 ppb. It has been noted that these MDLs for DC-5772 are imprecise and lack the statistical significance necessary for fate and effect studies. The more appropriate MDLs for DC-5772 would range from 1.6-6.4 ppm.
- o Examination of the active ingredient of DC-5772 would indicate that total silicon is not the best portion of the molecule to monitor for the presence of DC-5772. Perhaps, another functional group of the organic molecule would serve as a better measure of the active ingredient (e.g., aminodimethyl). Perhaps, radiolabeling of the molecule at

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MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

strategic atoms would more easily enable monitoring of the hydrolysis of the molecule. The exact change in the concentration of the active ingredient could be better determined. In addition, the state and concentration molecule could be determined by more specific analytical detection system(e.g., high performance liquid chromatography (HPLC)/electrochemical detection or ICP-MS).

- o It is also important to know the concentrations of the contaminants present in the test solutions (i.e., [REDACTED] and methanol); these were not determined by ABC Laboratories.

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### PART III

#### CONCLUSION

We think that the present method for the determination of the active ingredient in a buffered aqueous solution of DC-5772 by ICP is inadequate to obtain the information necessary for the proper evaluation of the fate and effects of this product because it is imprecise and the detection limit is not sensitive enough to measure at the predicted effects concentrations. Additional study will be required to ascertain a better methodology.

**DRAFT****OVERVIEW OF ECME 0059 - W1****DOW CORNING® 5772 ANTIMICROBIAL AGENT**

**A review of the Analytical Bio-Chemistry Laboratories (ABC Labs) report:**

**Study Title - "Hydrolysis of DC-5772 as a Function of pH"** indicated that ABC laboratories found that Dow Corning® 5772 Antimicrobial Agent (DC-5772) [also known as Dow Corning® Q9-6346 Silane] undergoes rapid hydrolysis in water (half-lives ranging from approximately 4 to 15 minutes, pH dependent). The data provided in the report also indicated an inherent problem in the measurement of the concentration of total-silicon (Si) using inductively coupled plasma spectroscopy (ICP) in the test aqueous solution of DC-5772 solution due to the presence of excessive background levels of total-Si in the preparative deionized and reconstituted hard waters. Background concentrations of total-Si in deionized water and reconstituted hard water were approximately 200 and 400 parts-per-billion (ppb), respectively. This is of particular concern due to the low toxicity concentrations [i.e.  $EC_{50}$  (rainbow trout) = 6 ppb;  $EC_{50}$  (Daphnia) = 32 ppb].

**There are several problems with the data which should be resolved:**

- The sample concentrations of silicon (Table XI) vary for the three replicate analyses at the time intervals at the given pH: (the %RSD range from 7.3 to 57.1%).
- The sample concentrations of silicon do not compare very favorably with the estimated values as determined by  $^1\text{H-NMR}$  at approximately the one hour hydrolysis stage.
- Examination of the linear regression curve for the NIST (#3150-Si) standard would indicate that the detection limit would be approximately 100-200 ppb.
- If ABC Laboratories is aware of the background interferences due to silicon in solution and has determined these levels to be 200 ppb in deionized water and 400 ppb for reconstituted hard water, then it is difficult to validate its calculated method detection limit of 13-37 ppb (40 CFR 136 Appendix B).
- In Procedural Step 7 of 40 CFR 136 Appendix B, there an optional iterative procedure to verify the reasonableness of the estimates of the MDL and subsequent MDL determinations. In the case of the siloxanols and siloxanes of the DC-5772, the background interference of the aqueous solutions would indicate that additional verification of the MDLs (13-37 ppb) is necessary.
- The recommended wavelength and estimated instrumental detection limit for silicon (as  $\text{SiO}_2$ ) was 58  $\mu\text{g/l}$  (ppb) at 288.158 nm [40 CFR 136 Appendix C. Inductively Coupled Plasma - Atomic Emission Spectrometric Method for Trace Element Analysis of Water and Waste Methods 200.7). The calculated range of the MDL for DC-5772 (as Si) was 13-37 ppb. This appears to be an area of conflict that should be resolved.
- Examination of the active ingredient of DC-5772 would indicate that total silicon is not the best species to monitor for the presence of DC-5772. Perhaps, another functional group of the organic molecule would serve as a better measure of the active ingredient. A review of the analytical literature could answer this question.
- The  $EC_{50}$  (DC-5772-Si) in rainbow trout is 6 ppb. The lowest observable effect concentration (LOEC) (DC-5772-Si) is 4 ppb. This is a very low concentration for toxicity and it is comparable freshwater concentrations of Aldrin (3 ppb), cadmium (3.9 ppb), Dieldrin (2.5 ppb), mercury (2.4 ppb), and polychlorinated biphenyls (2.0 ppb). If these levels are true, then it is

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critical that these concentrations be measured accurately.

- Perhaps, it is not the active ingredient of DC-5772 that is the cause of this toxicity. It is important to ascertain all effects of the active ingredient and any by-products and inert ingredient and their mode of entry.
- There should be a review of the most recent scientific literature to determine any new, more sensitive methods for the determination of silicon in aqueous solutions.



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

MAR 5 1996

CERTIFIED MAIL Z 069 418 021

Dr. David E. Powell  
Dow Corning Corporation  
P. O. Box 994  
Midland, Michigan 48686-0994

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

Subject: Review of submission for Case 3148, A. I. 107401, Dow Corning 5772 Antimicrobial Agent. Analytical Method, "Hydrolysis of DC-5772 as a Function of pH".

Dear Dr. Powell,

This letter constitutes the Agency's review and determination of acceptability of the method, "Hydrolysis of DC-5772 as a Function of pH".

The present method for the determination of the active ingredient in a buffered aqueous solution of DC-5772 by Inductive Coupled Plasma spectroscopy is inadequate to obtain the information necessary for the proper evaluation of the fate and effects of this product. This method is imprecise and the detection limit is not sensitive enough to measure at the predicted effects concentrations. Additional study will be required to ascertain a better methodology.

A revised method to determine the hydrolysis rate (Guideline 161-1), and aquatic toxicity (Guideline 72-1c and 72-2a) of Dow Corning 5772 antimicrobial agent, must be submitted by June 1, 1996.

If you do not submit the data within the specified time frame, I may pursue the appropriate regulatory action to ensure compliance with our statutory goals. If you have any questions regarding this letter, please contact Leonard Ryan in the Accelerated Reregistration Branch at (703) 308-8067.

Sincerely,

Jay Ellenberger, Chief  
Accelerated Reregistration Branch  
Special Review and  
Reregistration Division

Enclosure

cc: Aubry Dupuy, Jr. BEAD  
Marion Johnson, Jr. RD



13544

R107026

**Chemical:** 1-Octadecanaminium, N,N-dimethyl-N-(3-(t

**PC Code:** 107401

**HED File Code:** 61200 SRRD CDC

**Memo Date:** 06/16/95

**File ID:** 00000000

**Accession Number:** 412-05-0097

**HED Records Reference Center**  
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