

Isocyanurate Industry Ad Hoc Committee

Manager: Pesticide Registration Associates, D.C.

715 Eighth Street, S.E., Suite 3, Washington, D.C. 20003-2802

Phone: 202-546-3260 FAX: 202-546-3262 E-mail: geripest@aol.com

May 20, 2004

Administrator Michael O. Leavitt
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116
Attention: Chemical Right-to-Know Program
Via E-mail: oppt.ncic@epa.gov and chem.rtk@epa.gov

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**RE: Isocyanurate Industry Ad Hoc Committee Response to EPA Comments
on Trichloro-s-triazinetriene (CAS No. 87-90-1)**

Dear Administrator Leavitt:

On behalf of the Isocyanurate Industry Ad Hoc Committee (IIAHC), I am pleased to respond to the Agency's letter of December 31, 2003, providing EPA's comments on the robust summaries and test plan for Trichloro-s-triazinetriene (CAS No. 87-90-1). Members of IIAHC supporting this submission include:

- Aqua Clor, S.A. de C.V., Monterrey, N.L., C.P. 64070 MEXICO
- Aragonasas DELSA, SA (DELSA), 28004 Madrid, SPAIN
- BioLab, Inc., Lawrenceville, GA 30049
- Clearon Corporation, Fort Lee, NJ 07024
- Fertilizers & Chemicals, Ltd., Haifa 3 1013, ISRAEL W CE
- ICI Americas, Inc., Bridgewater, NJ 08807
- Nissan Chemical America Corporation, Houston, TX 77042
- Nisso America, Inc., New York, NY 10017
- Occidental Chemical Corporation, Dallas, TX 75380
- Shikoku Chemicals Corporation, Orange, CA 92668

The attached contains an explanatory response to each of the issues raised by EPA as well as a revised compilation of robust summaries. The IIAHC believes that this supplemental response further reinforces our earlier conclusion that the available data adequately characterize each SIDS endpoint. Moreover, these data reinforce the view

Administrator Michael O. Leavitt
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that there is sufficient information to justify the continued safe use of these products for their intended applications.

If there are questions, please contact me at 678-502-4127 or Geri Werdig at 202-546-3260.

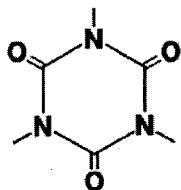
Sincerely,

Gary A. Wright, Ph.D.
IIAHC HPV Review Committee,
Chairman

Enclosures:

- 1) IIAHC Explanatory Response to EPA Comments on HPV Submission for Trichloro-s-triazinetriene (CAS No. 87-90-1)
- 2) Revised Robust Summaries for Trichloro-s-triazinetriene

cc: Mr. Oscar Hernandez, Director, Risk Assessment Division
Mr. Richard Hefter, Jr., Chief, HPV Branch
Ms. Geraldine W. Werdig, Manager, IIAHC
Mr. Robert J. Fensterheim, RegNet



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RESPONSE TO EPA COMMENTS ON HPV SUBMISSION FOR TRICHLORO-S-TRIAZINETRIONE (CAS No. 87-90-1)

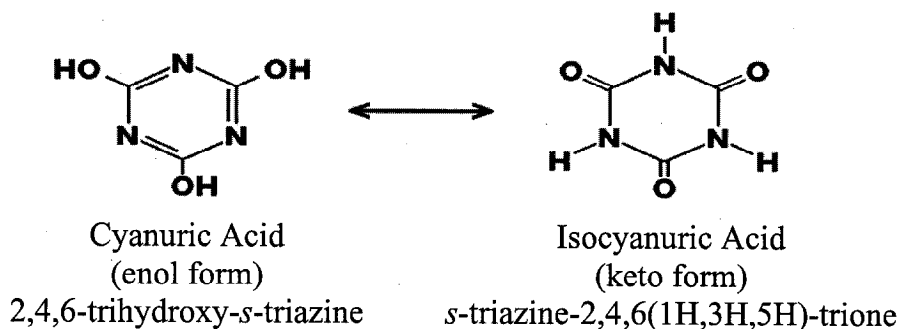
May 20, 2004

The following responds to EPA's comments on the test plan and robust summaries submitted by the Isocyanurate Industry Ad Hoc Committee (IIAHC) for trichloro-s-triazinetriene (CAS No. 87-90-1). An explanatory response is provided for each of the specific comments raised by EPA. Also, a revised and updated set of robust summaries is attached. This includes several new robust summaries that were prepared partly to address EPA's comments.

I. BACKGROUND ON CHLORINATED ISOCYANURATES

The chlorinated isocyanurates are chlorinated derivatives of isocyanuric acid ($\text{H}_3\text{C}_3\text{N}_3\text{O}_3$). The structures of the various isocyanurates are normally discussed in terms of the two tautomers (see structures below) that serve as the basis for their nomenclature. The keto form (isocyanuric acid) is present in the solid state or acidic solution, but in alkaline solution, the anions formed are derived from the enol tautomer. The enol tautomer shown below does not really exist as such in solution, rather it is the parent structure for the deprotonated forms which exist at higher pH's. While regulatory agencies and the scientific literature generally use the triazine nomenclature, the isocyanurate designations are preferred in commerce.

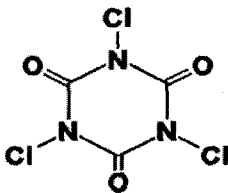
Chemical Structure of (Iso)cyanuric Acid Tautomers



The structure of 1,3,5-trichloro-s-triazine-2,4,6(1H,3H,5H)-trione is given below. The chlorine atoms are attached to the nitrogen atoms, replacing the protons in isocyanuric

acid. Thus, the chlorinated derivatives are considered to be derivatives of *s*-triazine-2,4,6(1H,3H,5H)-trione.

Chemical Structure of 1,3,5-trichloro-*s*-triazine-2,4,6(1H,3H,5H)-trione



The chlorinated isocyanurates hydrolyze in water to produce free available chlorine (chlorine in the +1 oxidation state) in the form of hypochlorous acid (HOCl). Activity of the chlorinated isocyanurates is often measured in terms of the available chlorine content.

II. ISOCYANURIC ACID SHOULD BE CONSIDERED RELEVANT TO ASSESS THE ENVIRONMENTAL IMPACTS

In its comments on the test plan, EPA requested additional information on the hydrolysis of the trichloro-*s*-triazinetriene and any other information that could be used to support the use of isocyanuric acid in the test plan. To address EPA's comments, IIAHC is submitting three new robust summaries that provide supplemental information on the water stability of the chlorinated isocyanurates.

Nonetheless, it is important to clarify that in submitting data on isocyanuric acid (cyanuric acid), IIAHC was not representing this substance as a "surrogate" (*i.e.*, a compound that can be used to estimate the characteristics or effects of other compounds). Rather, isocyanuric acid released from the chlorinated isocyanurates is the most biologically relevant and stable substance from the use of these products.

Isocyanuric acid is the parent compound for all the chlorinated isocyanurates. Once the chlorinated isocyanurates are dissolved into water, the compounds rapidly hydrolyze to release free available chlorine in the form of hypochlorous acid. A series of equilibrium reactions occurs which may result in six chlorinated and four non-chlorinated isocyanurate substances. The relative concentrations of the particular compounds depend on the pH, temperature, the initial chlorinated isocyanurate concentration, and the presence of other substances in the water.

To further illustrate and substantiate this characteristic of the release of isocyanuric acid from the chlorinated isocyanurates, additional summaries have been prepared that are included in the Revised Robust Summaries document. The three additional summaries review: 1) the stability of the chlorinated isocyanurates in clean water, including data on the hydrolysis equilibrium constants and hydrolysis rates; 2) the stability of the chlorinated isocyanurates when released into the environment, in particular, when released into natural waters which contain substances that rapidly reduce free chlorine ("chlorine demand"); and 3) the stability of the chlorinated isocyanurates when ingested.

Given the extremely short half-life of chlorinated isocyanurates in water, the IIAHC maintains that test data on the more stable isocyanuric acid (CAS No. 108-80-5) or its sodium salt (CAS No. 2624-17-1) are appropriate for purposes of assessing the environmental and toxicological properties of trichloro-s-triazinetriene. This is the same approach used by EPA to support the FIFRA registration of these chlorinated isocyanurates, including use in the Reregistration Eligibility Decision (RED) document. As such, test data on isocyanuric acid should be considered relevant and adequate for assessing the environmental toxicity profile and the health effects of the chlorinated isocyanurates.

III. RESPONSE TO SPECIFIC ISSUES

A. Environmental Fate and Effects

1. Melting point /boiling point.

EPA: For data entry purposes, the submitter needs to provide a separate robust summary for each endpoint.

IIAHC RESPONSE: As requested, separate robust summaries have been developed for melting point and boiling point, and are included in the revised set of Robust Summaries.

2. Vapor pressure

EPA: The submitter provided two open-ended values for this endpoint (<1 mm Hg, and less than 0.002 Pa). Open-ended values are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide a specific value for this endpoint, unless precluded by experimental obstacles.

IIAHC RESPONSE: There is now one robust summary on vapor pressure, which reports a value of less than 0.002 Pa (less than 0.000015 mm Hg). A more precise value is not feasible given limitations with the available analytical methods.

3. Environmental Fate (photodegradation, stability in water, biodegradation, transport and distribution (fugacity))

EPA: Adequate data are available for photodegradation, biodegradation, and transport and distribution for the purposes of the HPV Challenge Program, provided the submitter can justify the use of surrogate data on isocyanuric acid and monosodium cyanurate.

IIAHC RESPONSE: For the reasons described above, data on isocyanuric acid should be considered appropriate for assessing the environmental fate of these compounds.

4. Stability in water

EPA: The submitter indicates in the test plan cover letter that the chlorinated isocyanurates hydrolyze to form isocyanuric acid and free available chlorine, undergoing equilibria to form chlorinated and non-chlorinated isocyanurates. However, the robust summary indicates that this chemical is unstable in the environment because "the available chlorine is rapidly reduced," and that cyanuric acid is the degradation product. The submitter needs to explain this point in more detail to reconcile the information in the test plan and robust summary.

The submitter also needs to provide data on the reaction rate of trichloro-s-triazinetriene in water to clarify the significance of the reactions and the reasonableness of the proposed approach to justify the use of isocyanuric acid and sodium cyanurate monohydrate as surrogates of their trichloro- analog. The ability to isolate sodium dichloro-s-triazinetriene dihydrate is also unexplained with respect to the purported instability of trichloro-s-triazinetriene.

IIAHC RESPONSE: Additional robust summaries have been prepared to describe the stability in water of the chlorinated isocyanurates. Furthermore, as requested by EPA, additional information on the reaction rates in water is presented to support the use of isocyanuric acid and sodium cyanurate monohydrate as the relevant compounds of interest. The new summaries (7a, 7b and 7c) show that exposures from the use of chlorinated isocyanurates in water quickly result in isocyanuric acid or its salt. Therefore, isocyanuric acid is the primary substance of toxicological and environmental interest, not simply a "surrogate" substance.

Hydrolysis is an equilibrium reaction, not an irreversible reaction. Therefore, at the low (mg/L) concentrations at which the chlorinated isocyanurates are typically used, these materials are dissociated to a very large extent. However, at the very high concentrations at which they are manufactured, either trichloro-s-triazinetriene or sodium dichloro-s-triazinetriene dihydrate (depending on pH) exist at high enough concentrations to be isolated to produce these products.

5. Ecological Effects

EPA: Adequate data are available for fish and invertebrates for the purposes of the HPV Challenge Program. The submitter did not provide alga data that measured biomass or growth rate using appropriate test guidelines. Therefore, the submitter needs to conduct a 72- or 96-hour algal study on trichloro-s-triazinetriene to determine growth rate or biomass according to OECD TG 201.

IIAHC RESPONSE: Chlorine is long recognized as an algaecide. Under EPA's FIFRA registration program, chlorinated isocyanurates are approved for use as algaecides given that they are an effective source of free chlorine. As such, additional studies to evaluate the toxicological properties of any of the chlorinated isocyanurates on algae are not warranted. Testing with isocyanuric acid is provided in the robust summaries and

indicates that this substance has low toxicity to algae and is not of environmental concern from the use of chlorinated isocyanurates.

B. Health Effects

1. Health Effects

EPA: Adequate data are available for all endpoints for the purposes of the HPV Challenge Program, provided the submitter can justify the use of surrogate data on isocyanuric acid and monosodium cyanurate for the genetic, reproductive and developmental toxicity endpoints.

IIAHC RESPONSE: In order to assess the adequacy of the mammalian toxicity information, it is important to recognize that there is limited opportunity for exposure to chlorinated isocyanurates, both occupationally and with residential uses.

To the extent there is incidental oral ingestion, the chlorinated isocyanurates will rapidly dissociate to chloride ions and isocyanuric acid. This rapid dissociation starts as the compounds come in contact with saliva and then continues at an even faster rate in the stomach. Complete dissociation is expected to occur in less than a few seconds.

As soon as the chlorinated isocyanurates come in contact with saliva (pH=7), they begin to hydrolyze to release free chlorine in the form of hypochlorous acid (see Robust Summary 7a). As demonstrated by Scully and White (Robust Summary 7c), the hypochlorous acid rapidly reacts with the sulfur-containing amino acids, thiocyanate, as well as other compounds in saliva to form chloride ion and unchlorinated oxidation products. The reactions in saliva are fast enough and the chlorine demand is high enough such that all of the free chlorine in typical drinking water is destroyed as the water is swallowed. The half-life for the reaction with thiocyanate at pH 7 is about 0.01 seconds. There is enough thiocyanate in saliva to consume about 20 mg/L of free chlorine in 15 ml of water (or 2 mg/L of free chlorine in 150 ml of water).

Assuming that any of the chlorinated isocyanurates survive past the mouth, there is even greater dissociation in the stomach due to the lower pH of the stomach acids (pH=2-3). Also, the chlorine demand in the stomach is higher (about 500 mg/L). For these reasons, assessing the toxicity of the chlorinated isocyanurates following ingestion is best represented by the toxicity of free chlorine and isocyanuric acid. Therefore, exposures from the use of chlorinated isocyanurates in water and any incidental consequent oral ingestion will result in isocyanuric acid, which is considered the primary substance of toxicological interest rather than simply a "surrogate" substance.

It is relevant to note that the use of data on free chlorine and isocyanuric acid to assess the toxicity of the chlorinated isocyanurates is consistent with the approach that EPA used in support of the FIFRA registration of these compounds. As stated in the RED, EPA concluded that since the toxicological effects of chlorine are well known, isocyanuric acid can represent all the chlorinated isocyanurates for the purpose of conducting metabolism, subchronic, chronic, developmental, and mutagenicity studies.

EPA further noted that using isocyanuric acid as the test substance would allow for a distinction to be made between the toxicological effects of the triazinetrione moiety from those of chlorine. Since sodium isocyanurate was considered to be toxicologically equivalent to isocyanuric acid, it was determined to be a suitable test substance.

2. Acute toxicity

EPA: The submitter needs to provide additional information on clinical signs in the first oral study (CAS No. 87-90-1) so that results can be compared with the oral study on CAS No. 108-80-5.

IIAHC RESPONSE: The robust summary for the acute oral toxicity of s-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-trichloro- (CAS No. 87-90-1) has been revised to include information on the clinical signs reported in the study. Since the acute toxicity of the chlorinated isocyanurates is significantly different from isocyanuric acid, there is little value in comparing the observed effects. For example, the LD50 value determined for isocyanuric acid is >5000 mg/kg, while the LD50 values for the chlorinated isocyanurates are much lower due to the recognized toxicological properties of chlorine which is immediately released following exposure.

While test data on the chlorinated isocyanurates are relevant to assess the effects from acute exposure, due to the rapid dissociation of these compounds, the toxicological properties from repeat exposures are best represented by the properties of chlorine and the properties of isocyanuric acid. Since the toxicity of chlorine is well established, we have retained the Robust Summary for the acute oral toxicity study of isocyanuric acid as an additional point of reference.

3. Developmental toxicity

EPA: In the study by Springborn Laboratories, Inc. (18b), the submitter needs to provide additional data on the historical controls for post-implantation losses (e.g., dates for the control data are needed to confirm that they are recent and the laboratory should be specified to confirm that the studies were conducted at the same laboratory).

IIAHC RESPONSE: The robust summary for the developmental toxicity study in rabbits conducted at Springborn Laboratories has been revised. The historical control data on post-implantation losses, as cited in the full study report, have been added to the robust summary. While the control data collection dates are not specified, they are believed to have been generated from the same laboratory during a time period approximate to the isocyanurate study and therefore should be considered relevant.