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**STABILITY OF EXEMPT CHEMICAL SURETY MATERIEL (XCSM) IN COMMONLY
USED DILUENTS UNDER ROUTINE STORAGE CONDITIONS**

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94-08703

ABSTRACT

Due to either the extreme toxicity of chemical surety materiel (CSM) or the limitations of the experimental facility, it is often required that CSM be diluted before use. The requisite of selecting both a non-toxic diluent and a diluent that does not bias the proposed experiment often results in use of "non-standard" analytical solvents. These "non-standard" solvents include distilled water, drug vehicles, and culture media. The lack of sufficient agent/solvent stability information in these solutions is of major concern to both experimental designers and data reviewers.

The objectives of this task were to determine the shelf life of exempt concentrations of GA, GB, CD, VX, and HD in selected diluents at prescribed concentrations and temperatures, and to assemble this information into a database. Efforts included the development of analytical methods necessary to perform these stability experiments and the compilation of results into a working database. The database, once completed, will be made available to XCSM researchers and will be updated as necessary.

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INTRODUCTION

This effort is to determine the shelf life of various concentrations of exempt chemical surety materiel (XCSM) in commonly used diluents under

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selected storage conditions. The confirmation and documentation of the stability of dilute chemical surety materiel (XCSM) used as dosing solutions for toxicology and pharmacology studies is essential.

The requirement that dilutions be made, either for improved accuracy in dose delivery or increased safety in the handling of the materiel, often leaves the researcher with limited choices. Since most analytical diluents commonly used for gas chromatography (GC) are too toxic for biological testing, a final aqueous-based solvent is often selected for biological tests. This presents a dilemma in that the researcher must determine, for each diluent/CSM combination, (1) storage time under the experimental requirements and (2) available storage conditions with negligible loss in CSM potency. Performing dilute solution dosing experiments requires some knowledge of shelf life of the solution and an analytical method suitable for stability confirmation.

Although stability data do exist for some agent/solvent combinations, a compilation of quality data could not be located in a literature search. Much of the data that were available were performed secondary to the research being performed and, therefore, were not reported in sufficient detail to determine the validity of the data. When completed, this task will provide a shelf-life database that can be referenced whenever dilute solutions are prepared for storage or use. The database established during this effort will be a compilation of experimentally derived data and will serve as a foundation on which to build a comprehensive agent/solvent stability database. Emphasis has been placed on database structure, so researchers may query and update the database as new information is acquired.

METHODS

The separation and detection technique most commonly used in our laboratory for the quantitative measurement of XCSM solutions is GC with a selective detector⁽¹⁾. This methodology provides for a more accurate method of determining the concentration of agents in the presence of degradation products than detection methods that do not provide for a chromatographic separation of the agents and interfering materials.

The stability studies conducted involve several parameters. The preliminary set of agents and solvents are:

- GA - Hexane, Chloroform, Distilled/Deionized Water, Multisol
- GB - Hexane, Chloroform, Distilled/Deionized Water
- GD - Hexane, Chloroform, Distilled/Deionized Water
- VX - Hexane, Chloroform, Distilled/Deionized Water
- HD - Hexane, Chloroform, Ethanol, Methylene Chloride
- L - Hexane, Chloroform, Ethanol

The agent/solvent combinations listed are to be studied under several storage temperature conditions. The storage temperatures selected for the initial phase were those commonly used in USAMRICD and MREF protocols or

SOPs. The initial storage temperatures are:

- 70 C (long-term storage conditions)
- 4 to 7 C (short-term storage conditions)
- 22 C (room temperature)
- 37 C (body temperature)

In addition to the parameters of agent, solvent, and temperature, the effects of concentration are also being evaluated. Three concentrations of dilute agent solutions were selected: 99 percent, 10 percent and 1 percent of surety concentration for each agent. The agent preparations for this effort are formulated using neat SARM materials and the appropriate spectroscopic grade solvents. The samples are prepared individually in a quantity large enough so that at least 20 samples can be stored for assay during the shelf-life study. Once samples are prepared at the appropriate dilution, the stock solutions are packaged in individual vials and immediately stored under the appropriate temperature conditions. At selected time intervals, a vial is removed and analyzed for concentration. The resultant data are archived in a database for subsequent statistical analysis for half-life values.

Each of the listed parameters is being evaluated separately, with the results being compiled for each parameter combination and entered into the database. From these data, an estimate of the decay rate will be calculated. The experimental data are being collected over a period of 6 months of storage or until a 70 percent decomposition of CSM has been observed. The data are being compiled in a database developed to easily accept changes and new information.

RESULTS AND DISCUSSION

The goal of this effort is to produce a reference document that contains both a summary of the published chemical data for each of the agents to be evaluated and the shelf life of exempt concentrations of GA, GB, GD, VX, and HD in prescribed diluents and stored at prescribed concentrations and temperatures. This document will provide a shelf-life database that can be used as a reference whenever dilute solutions are prepared for storage or use. Examples of the proposed format to be used for summarizing the chemical data is presented in Figures 1 and 2 for GD and HD, respectively. This information is derived from various sources including the MSDSs provided by USAMRICD with the CSM.

The shelf-life database is being constructed from the analytical data collected for each of the listed agent/solvent combinations. Once either the maximum storage time of six months or 70 percent degradation has been reached, the data are analyzed. The statistical analysis consists of fitting models to the concentration-time data for each combination of agent, diluent, temperature, and concentration to estimate the relationship between percent XCSM remaining and time. Residuals from fitted models and plots of the percent of XCSM remaining data are used to select the form of the model most appropriate for each CSM. Models considered include linear, first order exponential, second order exponentials, and logistic rates of decay.

FIGURE 1. SUMMARY OF CHEMICAL DATA FOR SOMAN FROM LITERATURE

CHEMICAL SURETY MATERIEL

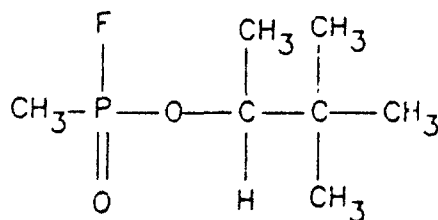
SOMAN (GD)

Synonyms: EA 1210, Zoman, PFMP

CAS Registry Number: 96-64-0 or 50642-24-5

Chemical Family: Fluorinated organophosphorus compound

Structural Formula: Empirical Formula: $C_7H_{16}FO_2P$



Pinacolyl methyl phosphonofluoridate

Molecular Formula: $CH_3P(O)(F)OCH(CH_3)C(CH_3)_3$

Molecular Weight: 182.178

Freezing Point: $-42^{\circ}C$

Liquid Density: 1.0222 at $25^{\circ}C$

Boiling Point: $198^{\circ}C$

Vapor Pressure: 0.40 mm Hg at $25^{\circ}C$

Volatility: 3900 mg/m³ at $25^{\circ}C$

FIGURE 2. SUMMARY OF CHEMICAL DATA FOR SULFUR MUSTARD FROM LITERATURE

CHEMICAL SURETY MATERIEL

SULFUR MUSTARD (HD)

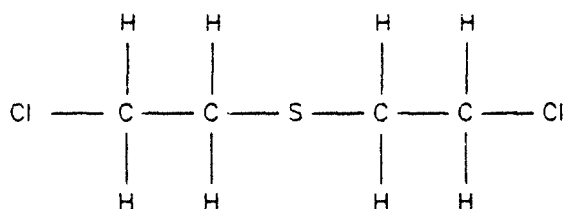
Synonyms: Senfgas, Yperite, bis (2-chloroethyl)Sulfide

CAS Registry Number: 505-60-2, 39472-40-7, or 68157-62-0

Chemical Family: Chlorinated sulfur compound

Structural Formula:

Empirical Formula: $C_4H_8Cl_2S$



2,2'-dichloroethyl sulfide

Molecular Formula: $ClCH_2CH_2SCH_2CH_2Cl$

Molecular Weight: 159.08

Freezing Point: $14^{\circ}C$

Liquid Density: 1.27 at $20^{\circ}C$

Boiling Point: $217^{\circ}C$

Vapor Pressure: 0.072mm Hg at $20^{\circ}C$
0.11 mm Hg at $25^{\circ}C$

Volatility: 610 mg/m^3 at $20^{\circ}C$
920 mg/m^3 at $25^{\circ}C$

The estimated parameters from the statistical modeling are then used to calculate the time at which the solutions decay to 50 and to 90 percent of their initial concentration. Examples of the agent stability data are presented in Figures 3 and 4.

CONCLUSIONS

When completed, this program will provide researchers with a compilation of reference information to assist in the selection of storage solvents and conditions, along with an archived database that can be updated as information becomes available. The database will use a standard conventional database structure, so information acquired can be added, thus producing a working database. The database will be made available through the U.S. Army for future reference and updating as new information is collected.

REFERENCES

- (1) Hayes, T.L., Reeves, M.L., Arp J. C., Chelwick, T.J., Cunningham, R.I., Joiner, R.L., Dill, G.S.; Development of a Gas Chromatographic Analytical Method for Detecting CSM in Aqueous Solutions; Proceeding of the 1989 Medical Defense Bioscience Review; 15-17 August 1989.

FIGURE 3. EXAMPLE OF SHELF LIFE DATA FOR REFERENCE DOCUMENT

AGENT: GD DILUENT: DISTILLED WATER STORAGE TEMP: +5°C

Percent Amount Remaining of Prepared Concentration of
GD tested at +5 °C in Distilled Water

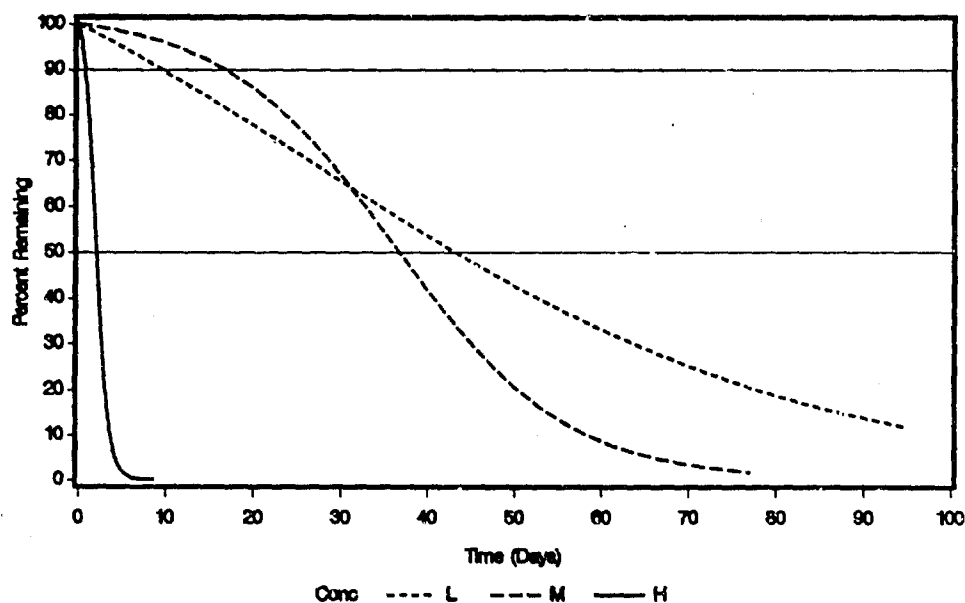


TABLE 1. TIME TO DEGRADATION AND ESTIMATED HALF LIVES FOR GD IN DISTILLED WATER AT +5 DEGREES C

Prepared Conc mg/mL	Maximum Time Analyzed (Days)	Measured Initial Conc. (mg/mL)	Measured Minimum Purity (Percent)	Estimated Time to 90% Purity (Days)	Estimated Half Life (Days)
L - 0.0198	95	0.0120	1.7	9.4	43.1
M - 0.198	77	0.198	1.5	16.6	36.7
H - 1.98	9	2.01	0.0	0.7	2.0

FIGURE 4. EXAMPLE OF SHELF LIFE DATA FOR REFERENCE DOCUMENT

AGENT: HD DILUENT: ETHANOL STORAGE TEMP: +37°C

Percent Amount Remaining of Prepared Concentration of
HD tested at +37 °C in Ethanol

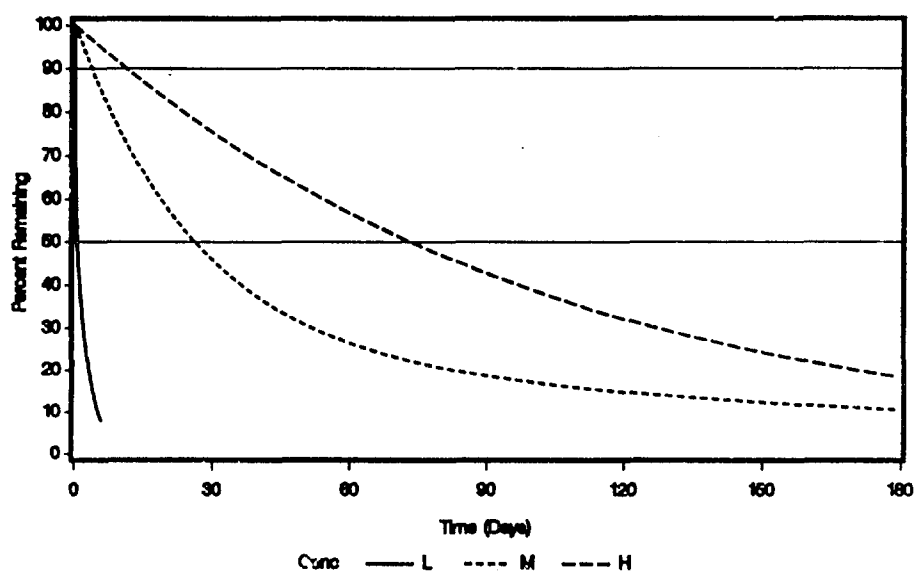


TABLE 2. TIME TO DEGRADATION AND ESTIMATED HALF LIVES FOR GD IN DISTILLED WATER AT +37 DEGREES C

Prepared Conc mg/mL	Maximum Time Analyzed (Days)	Measured Initial Conc. (mg/mL)	Measured Minimum Purity (Percent)	Estimated Time to 90% Purity (Days)	Estimated Half Life (Days)
L - 0.0198	6	0.111	6.9	0.0	0.6
M - 0.198	181	0.962	3.8	3.6	26.1
H - 1.98	181	9.18	22.2	11.1	73.2