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E.A.T.R. 341, COPY NO. 1.

(Project: A 3.3-1)

CYANOGEN CHLORIDE

EATR 341

Part I. Preparation.

By: Albert Morrison

Part II. Toxicity: Median Lethal Concentration for Mice.

By: S. D. Silver
F.P. McGrath

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CYANOGEN CHLORIDE.

Part I. Preparation.

Part II. Toxicity: Median Lethal Concentration for Mice.

ABSTRACT

Object.

One of the objects of project A 3.3-1 is to "reinvestigate the toxicity of cyanogen chloride under the latest conditions for conducting animal experimentation and establish the minimum lethal concentration for 2 minutes, for 10 minutes, and for 30 minutes".

The object of the work described in this report was to synthesize pure cyanogen chloride, to study the literature pertaining to its wartime use and to its stability and chemical constitution, to determine its median lethal concentration for white mice exposed for 2 minutes, 10 minutes, and 30 minutes and observed for 10 days, and to compare the value of cyanogen chloride as a war gas with phosgene and hydrocyanic acid.

Results.

Preparation.

About 750 g. of pure cyanogen chloride was prepared.

Properties.

Data regarding the sample of cyanogen chloride submitted for toxicity tests were as follows:

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ABSTRACT (Cont'd.)

Appearance: Water-white, mobile liquid.
Quantity: 400 g.
Date of delivery: Jan. 31, 1941.

Physical constants:

	Found	Literature
Boiling point	13.8°C.	12.55 to 13.0°C.
Melting point	-7.05°C.*	-6.5 to -7.4°C.
Density, 0°C.	1.224	1.222

Chlorine content: 57.51% Calc. 57.68%

Literature Search.

Cyanogen chloride hydrolyzes in alkaline media and also in sufficiently acid media.

Cyanogen chloride is subject to polymerization. Reports regarding the conditions under which polymerization occurs are very contradictory.

The structure of cyanogen chloride is not accurately known.

Lethality to Mice.

2-Min. Exposure: Nine runs with white mice, using a 2-min. exposure and a 10-day observation period, gave the following results:

Nominal concn. mg./l.	Analytical concn. mg./l.	Fraction dead	Per cent deaths
1.37	1.30	0/20	0
1.52	1.43	0/20	0
1.67	1.51	2/20	10
2.40	1.83	4/20	20
2.68	2.36	0/20	0
3.11	2.81	12/20	60
3.21	3.03	15/20	75
3.88	3.24	13/20	65
4.42	3.56	20/20	100

* A melting point of -6.7 was obtained on a sample of higher purity.

ABSTRACT (Cont'd.)

10-Min. Exposure: Eight runs with white mice, using a 10-min. exposure and a 10-day observation period, gave the following results:

Nominal concn. mg./l.	Analytical concn. mg./l.	Fraction dead	Per cent deaths
0.34	0.35	0/20	0
0.51	0.45	0/20	0
0.59	0.50	3/20	15
0.67	0.65	1/20	5
0.67	0.58	4/20	20
0.73	0.58	9/20	45
0.85	0.80	17/20	85
0.87	0.82	19/20	95

30-Min. Exposure: Seven runs with white mice, using a 30-min. exposure and a 10-day observation period, gave the following results:

Nominal concn. mg./l.	Analytical concn. mg./l.	Fraction dead	Per cent deaths
0.08	0.09	0/20	0
0.18	0.18	0/20	0
0.36	0.34	1/20	5
0.39	0.33	8/20	40
0.46	0.40	13/20	65
0.50	0.41	6/20	30
0.56	0.48	19/20	95

Comparison with Phosgene and Hydrocyanic Acid.

The properties of cyanogen chloride have been compared with those of phosgene and hydrocyanic acid in the light of the project specification for Project A 3, Nonpersistent Agent.

Conclusions.

Part I.

1. Pure CNCl can be prepared by the $Zn(CN)_2$ method.

2. The data on the stability of CNCl are fragmentary and inconclusive. No fundamental studies on the mechanism of the polymerization reaction have ever been made.

3. Definite agreement as to the chemical constitution of CNCl has not been reached, but the most recent work favors the nitrile structure.

Part II.

4. The median lethal concentration of cyanogen chloride for mice, for an exposure period of 2 min. and an observation period of 10 days, is 3.1 mg./l., with an average deviation (for 5 runs) of 0.28 mg./l.

5. The median lethal concentration of cyanogen chloride for mice, for an exposure period of 10 min. and an observation period of 10 days, is 0.75 mg./l., with an average deviation (for 6 runs) of 0.027 mg./l.

6. The median lethal concentration of cyanogen chloride for mice, for an exposure period of 30 min. and an observation period of 10 days, is 0.46 mg./l., with an average deviation (for 5 runs) of 0.030 mg./l.

General.

7. Cyanogen chloride does not meet the characteristics required for a nonpersistent agent to a sufficient extent to warrant further development for this use.

Recommendations.

None, since no further development work on cyanogen chloride is contemplated.

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CYANOGEN CHLORIDE.

Part I. Preparation.

I. INTRODUCTION.

One of the objects of Project A 3.3-1, Nonpersistent Gas, CNCl (1941 project program) was to "reinvestigate the toxicity of cyanogen chloride under the latest conditions for conducting animal experimentation and establish the minimum lethal concentration for 2 minutes, for 10 minutes, and for 30 minutes".

The objects of part I of this report were (1) to synthesize pure cyanogen chloride for use in accurately determining its toxicity and (2) to study the literature pertaining to its wartime use and to its stability and chemical constitution.

II. HISTORICAL.

Cyanogen chloride was extensively investigated at the American University Experiment Station in 1918 (C.W.M. 24, chapter 1).

A search of the literature has indicated that cyanogen chloride was little used in the World War. Meyer, Der Gas Kampf, p. 401, states that "cyanogen chloride possesses a terrible odor and is lacrimatory and poisonous. Its limit of tolerance is 50 mg. per cubic meter of air. Its properties, however, do not seem to be such that it is suitable for use as a combat gas. It was used only by the French a few times by way of experiment, but with no success".

Rudolf Hanslian, Der Chemische Krieg, in the table of the most important chemical agents used in the World War, indicates that cyanogen chloride was used by the French, either by itself (mauguinite) or in admixture with arsenic trichloride (vitrite), and also by the Austro-Hungarians. No comment on the effectiveness of these agents was found.

A preliminary survey of the literature regarding the wartime use of cyanogen chloride was made at Edgewood Arsenal in 1926 by T. E. Knapp who was then Chief, Technical Library (E.T.F. 133-2). The following is quoted from his report:

"As far as I have been able to find, the French were the only ones to use cyanogen chloride in battle .....

"According to Report Z-210, June 25, 1918, the manufacture of Vincennite was being gradually abandoned owing to the persistent decline in the demands from the front. At that time the French placed great hopes in cyanogen chloride and believed that it would ultimately completely displace Vincennite. Also, at that time there were 82,000 projectiles filled with Vitrite (70% cyanogen chloride, and 30% arsenic trichloride), but in accordance with the policy of G.Q.G., no firing was to be done until at least 200,000 projectiles were ready and a daily output assured. At that time the production of cyanogen chloride amounted to a little over one ton per day, but when the new plant was ready to go at Rouen and with the improvements in the method of manufacture, this output was to be considerably increased. Six 75-mm. shells loaded May 7, 1917, containing Vitrite, were opened in July 1917 and in January 1918. 'The state of preservation of the mixture was found to be perfect in all shells examined.' Furthermore, the shells were not appreciably attacked. (Z-158, April 7, 1918.)

"According to Paterno, in Report Z-779, about December 1918, the Italians were favorably impressed with cyanogen chloride, although there is no evidence to show that they actually used it in battle. In this report reference is made to the fact that traces of acetic anhydride will overcome the great difficulty previously encountered with cyanogen chloride, namely, its polymerization. This report refers to rumors that the Germans used cyanogen chloride against the Russians, but there is no evidence to substantiate this. However, cyanogen bromide was actually identified in Austrian shells used against the Italians on July 9, 1916, the gas being used in 77-mm. shells. The Italians studied a number of mixtures of cyanogen chloride, but found that mustard, chloropicrin, and arsenic trichloride were the only substances tested which proved to form stable mixtures. They felt that the mixtures of cyanogen chloride and cyanogen bromide seemed to be best for practicable purposes.

"The British (A.G. 232, February 1918) studied the protection available against cyanogen chloride and found that the British respirator was satisfactory, but that the German respirator gave practically negligible protection. According to this report cyanogen chloride is definitely more toxic than hydrocyanic acid. However, later tests, reported in C.C.P. 622, December 2, 1918, led to an unfavorable view of the use of cyanogen chloride. This view was based upon field trials with cyanogen chloride. 'The work on this subject was not sufficiently promising to warrant further investigation.' The substance was found to have about the same order of toxicity as hydrocyanic acid. Its power of producing casualties in small concentrations was small. Concentrations could be set up which penetrated the German mask only when the material was used in drums. It had about the same power of penetration as the mixture of phosgene and cyanogen chloride. Before its consideration was finally dropped, it was decided to make a comparative test in drums of the penetrating powers of cyanogen chloride and phosgene, chloropicrin, and stannic chloride, and cyanogen chloride alone.

"The Americans conducted a number of experiments with cyanogen chloride, both in the laboratory and in field tests. Tests of 3-in. shell exploded in a bomb pit led to the conclusion that 'evidently cyanogen chloride undergoes but slight decomposition when exploded in 3-in. shell'. Field tests with Livens drums fired statically (A.M. 719) led to inconclusive results due to high wind. Another similar field test (P.T. 398) aimed at a comparison of the efficiencies of phosgene and cyanogen chloride and a mixture of the two. The results here indicated that mixtures of these two materials could not be recommended because 'the typical effect of one is minimized by dilution with the other'.

"From a study of binary mixtures of various materials (including cyanogen chloride) with particular reference to their penetration of the standard canister, the conclusion was drawn that no advantage was found in such mixtures over the equivalent quantity of the individual constituents.

"B.M. XXXVI-28, December 1918, is a monograph on Livens drums which states in regard to cyanogen chloride: 'Cyanogen chloride may be used as a filler for the Livens projectile. Its area of toxicity is roughly equal to that of phosgene when the temperature of the air is reasonably low and the temperature of the ground is not higher than that of the air. Cyanogen chloride is a lighter gas than phosgene and,

therefore, more sensitive to upward currents of air caused by the ground heating up to a temperature higher than that of the surrounding atmosphere. Under less favorable conditions of temperature and wind, the phosgene cloud behaves better. However, we believe that cyanogen chloride provides a substitute for phosgene worthy of some consideration. It produces death more quietly, and penetrates the German mask more rapidly."

More recently (1935), Armstrong and White (E.A.T.R. 191, Selection of a Quick-Acting Nonpersistent Agent) compared cyanogen chloride with other quick-casualty-producing nonpersistent agents and concluded that cyanogen chloride was second only to hydrocyanic acid among this group of agents.

In E.A.T.R. 269, Navy Liquid Lacrimator, Preliminary Investigation, by R. Macy, cyanogen chloride is listed among liquids which might be incorporated in a liquid lacrimator, but the concentration necessary to produce lacrimation in 50% of a large group of subjects is 40 times the concentration of chloroacetophenone required to produce the same result, and hence, no attempt was made to use cyanogen chloride in that work.

III. THEORETICAL.

Most methods for the preparation of cyanogen chloride involve essentially the action of chlorine on a solution or suspension of an inorganic cyanide or hydrocyanic acid in either an aqueous or a nonaqueous solvent. In the choice of a method, a primary consideration is the ease of elimination of certain contaminating materials, such as HCN, Cl_2, and HCl, that may induce polymerization to the solid trimer. The method of Jennings and Scott (J.Am.Chem.Soc. 41, 1241-8 (1919)), involving the action of chlorine on a suspension of NaCN (containing 2% H_2O) in CCl_4, seemed to satisfy this condition and hence was tried first. Experience, however, has shown that the method of chlorinating $Zn(CN)_2 \cdot 2NaCN$, as described in C.C.P. 5-69, pp. 65,173, was superior to that of Jennings and Scott. The reactions involved in this method are as follows:

$$(1) \quad 4NaCN + ZnSO_4 \longrightarrow Zn(CN)_2 \cdot 2NaCN + Na_2SO_4$$

$$(2) \quad Zn(CN)_2 \cdot 2NaCN + 2Cl_2 \longrightarrow Zn(CN)_2 + 2CNCl + 2NaCl$$

$$Zn(CN)_2 + 2Cl_2 \longrightarrow ZnCl_2 + 2CNCl$$

IV. STABILITY AND CONSTITUTION OF CYANOGEN CHLORIDE.

A. Stability.

The stability of CNCl has been studied and reported on extensively by Chemical Warfare Service investigators and to some extent by others. CNCl has a tendency to hydrolyze and to polymerize. It has long been known that hydrolysis is generally favored in alkaline media, although sufficiently high acid concentrations (equivalent to 10% HCN according to C.C.P. 5-69, pp. 98-100 or 9 N HCl according to J.Chem.Soc.Ind. 39, 100T (1920)) are similarly effective. Distillation experiments showed that water has little action on CNCl up to 20°C. and a surprisingly slow action at 40-100°C. (C.C.P. 5-69, pp. 103-4). Storage studies, however, on mixtures of CNCl and water indicated some decomposition (see following paragraph). Corrosive action on metals seems to depend usually on prior hydrolysis, since Fe, Pb, and Ag are reported to be unaffected by dry CNCl.

CNCl can be stored in steel containers without change (P.S. 433 and 605) unless impurities are present (C.C.P. 47 and 5-69, pp. 124-145). Observations were made of pressure changes and changes in composition and appearance in the presence of water, HCl, Cl, and polymerized CNCl. Water in excess of its saturation solubility (about 1% at 0° to -2°C.) produces large pressure increases and evolution of considerable CO_2. Similar studies were made (E.A.C.D. 11) with 75-mm. steel gas shells, and the following conclusions were drawn: CNCl can be stored for a year at room temperature in a steel shell without any difficulty. At 60°C. the contents remain stable for about nine weeks, but after that the gas becomes solid, probably as a result of polymerization. Only slight decomposition of CNCl results when 3-in. or 75-mm. gas shells are exploded (P.S. 366 and 474).

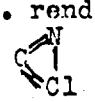
While numerous observations have been made on the polymerizing tendency of CNCl, there is poor agreement among them and there have been no fundamental studies on the mechanism of the reaction. According to O.R. 205, pure dry CNCl remains unchanged for five days and is unaffected by the presence of water and CCl_4, separately and in combination, for a similar period. Chlorine, both wet and dry, with or without CCl_4, produces slight polymerization after five days, with appearance of a slight yellow color. Dry HCl induces slight polymerization in five days, while wet HCl produces complete polymerization in a "short time". CNCl containing 10% HCN is less stable toward the above substances than is pure CNCl.

On the other hand, in C.C.P. 39 and 5-69, pp. 109-114, it is stated that a very high degree of purity appears unfavorable to stability and that when very pure dry CNCl is distilled, polymer tends to distill with it or forms in the distillate. The addition of about 3% water to dried CNCl increases its stability.

In the published literature (Ann. 287, 358 (1895); J.Am.Chem.Soc. 41, 1247-8 (1919); J.Soc.Chem.Ind. 39, 100T (1920)) there is agreement that pure CNCl does not polymerize, that Cl does not exert any polymerizing effect, and that dry HCl brings about marked polymerization. There is disagreement, however, as to whether traces of water induce polymerization or have no effect.

CNCl is reported to be stable in the presence of certain compounds; acetic anhydride in traces (Z-779), arsine (O.R. 60), and arsenic trichloride (Z-158 and Z-779), the last having been tried experimentally by the French. Moisture must be absent from CNCl-arsenic trichloride mixtures because it forms HCl, which hydrolyzes the CNCl with resulting danger of explosion (Z-150). A solution of chloroacetophenone and CNCl is claimed to be stable (P.S. 882), and also mixtures of mustard gas or chloropicrin with CNCl (Z-779). Pure $COCl_2$ does not react with pure CNCl, but if the agents are impure, cyanuric chloride and NH_4Cl are precipitated, and the reaction is hastened by iron (P.S. 880 and 881).

B. Constitution.

The chemical constitution of cyanogen chloride, which is naturally of interest in connection with a study of stability, has proved to be a troublesome question. For the most part, CNCl has been thought to have the structure of a nitrile, Cl-C≡N, or an isonitrile, Cl-N=C or Cl-N≡C. Nef (Ann. 287, 314-8 (1895)) and some other earlier workers (Gazz. chim. ital. 38, I, 97-8 (1908); Ann. 364, 69 (1909)) favored the nitrile structure, while still others drew some support for the isonitrile structure from refractive index and molecular dispersion studies (Bull. soc. chim. [4], 47, 453-7, 537-45 (1930)) as well as from chemical studies (J.Chem.Soc. 81, 192-6 1902)). Existence in the two isomeric forms has also been postulated: in a reactive form, Cl-C≡N, and an "inert" form, Cl-N≡C (J.Russ.Phys. Chem.Soc. 38, 1058-61 (1907); C.A. 1, 1268-9)), or in the gaseous state as Cl-N=C= and in the liquid state as Cl-C≡N (Compt. rend. 158, 457-61 (1914); C.A. 8, 1565)). A peroxide-like formula, 

was proposed (Ber. 42, 3623-8 (1909)) to account for the seeming dual nature of the compound and for its oxidizing action. More recently (Bull.soc.chim.[5], 1, 1544-6 (1934)), the chlorine atom has been characterized as an active or oxidizing halogen. It has been calculated from electron diffraction studies that 24% of $^{+}:\ddot{X}=C=\ddot{N}:^{-}$ is present in cyanogen halides in addition to the conventional electronic structure $:\ddot{X}-C\equiv N$ (J.Am.Chem.Soc. 61, 299-303 (1939)). However, spectroscopic and thermochemical data indicate that CNCl in the normal state is made up of normal chlorine atoms and normal cyanide radicals and that the structure is probably ClCN (J.Am.Chem.Soc. 53, 2572-7 (1931)). Studies of the Raman spectra of the cyanogen halides also lead to the conclusion that the nitrile structure is the correct one (J.Chem.Phys. 1, 402-5 (1933)).

V. EXPERIMENTAL.

A. Materials.

Crude CCl_4 was distilled for this purpose through an indented column fitted with a "cold finger" condensing head. The CCl_4 was collected at a constant-boiling temperature of 76°C., the small initial and tail fractions being discarded. The NaCN used was Baker-Adamson reagent grade. The chlorine was obtained from a cylinder. The $ZnSO_4$ was of unknown manufacture and purity.

B. Preparation of Cyanogen Chloride.

In the preparation of cyanogen chloride by chlorinating a suspension of NaCN in CCl_4 by the Jennings and Scott method, a 4-neck 2-liter flask was used, fitted with a thermometer well, a mineral oil-mercury-sealed mechanical stirrer, a condenser, and a tube for introducing chlorine fitted with a sintered glass disk for dispersing the gas. The chlorine was led, through a bubbler containing H_2SO_4, into the reaction mixture kept at 0° ± 5°C. with an ice-salt bath. When the chlorine absorption was complete, as indicated by gas passing through the bubbler on the end of the absorption train, the temperature in the reaction vessel was slowly raised to approximately 40°C. The product was distilled from the reaction vessel, passing through a condenser kept at 10-12°C., then through a column of moist marble chips, and finally through a $CaCl_2$ drying tower into a receiver surrounded by an ice-salt mixture maintained at 0° ± 5°C. The receiver opened to the atmosphere through another $CaCl_2$ drying tower and a gas-washing bottle containing an alkali solution. The apparatus is shown on Dwg. A21-45-1, (p. 16).

In the zinc cyanide method, a 5-liter reaction vessel was used (see sketch A 21-45-1). Other changes in the setup included a metal packing gland in place of the mercury seal for the stirrer, the installation of a trap containing glass wool to act as a foam breaker, and a condenser leading into the receiver. This second condenser was cooled by brine maintained at 0° ± 5°C. and circulated by a small mechanical pump. The ratio of 4 moles of NaCN to each mole of $ZnSO_4$ was used and each salt dissolved separately in a liter of water. The two solutions were mixed, with agitation, in the reaction vessel maintained at 0° ± 5°C. When the NaCN solution is first added to the $ZnSO_4$ solution, $Zn(CN)_2$ is precipitated, but on further addition of the NaCN solution the precipitate is dissolved, forming the complex $Zn(CN)_2 \cdot 2NaCN$. In the present instance a yellow flock remained in spite of the addition of NaCN in excess of the theoretical. This may be due to some impurity in the $ZnSO_4$ (the purity of which was unknown).

One run was made by the Jennings and Scott method and four runs by the $Zn(CN)_2$ method. The former method gave a yellow product highly contaminated with chlorine, while the latter method gave a water-white liquid in 3 runs. The fourth run yielded a yellowish liquid, which, when treated with NaCN and redistilled, gave a colorless product. The distillates obtained from the $Zn(CN)_2$ method were mixed and the whole distilled, yielding a water-white mobile liquid with an intense lacrimatory action. About 750 g. of CNCl was obtained by redistilling the last 4 runs shown in table 1.

Table 1

Description of Runs.

Run no.	Method used	Materials used: NaCN	Materials used: $ZnSO_4 \cdot 7H_2O$	Chlorination time	Temp.	Yield in	
		g.	g.	hr.	°C.	g.	%
1	Jennings & Scott	650	-	7	-5 to +5	18*	-
2	$Zn(CN)_2$	150	191	10	-5 " +5	90**	48
3	"	300	430	9	-5 " +5	253	67
4	"	300	430	9	-5 " +5	275	73
5	"	350	500	10	-5 " +5	222***	51

* Defective reaction flask caused loss of yield.

** Practice run, no attempt made to distill maximum yield.

*** Low yield and yellow product probably due to overchlorination.

C. Determination of Physical Constants.

The boiling point (12-13°C.) of the CNCl was determined by observing a thermometer placed in the path of the condensing vapors. To determine the melting point, a small sample of the CNCl was placed, together with a thermometer and ring-shaped agitator, in a large test tube, and the latter was imbedded in an ice-salt mixture. When the sample was approximately half crystallized the test tube was transferred to an ice water bath and the sample permitted to melt with agitation. A constant temperature reading of -6.7°C. obtained during the transition from the solid to the liquid state was taken as the melting point.* The density was determined as follows: A volume of CNCl at 0°C. was weighed and the density computed from the weight of the same volume of distilled water at 20°C. A value of 1.224 was obtained.

A sample was analyzed for its chlorine content and a value of 57.51% was obtained (calculated 57.68%).

VI. FINAL SAMPLE FOR TEST.

During the interim between the synthesis of CNCl and its delivery to the Medical Research Division the material (750 g. sample, page 8) was stored in a sealed glass flask in an ice chest. Some weeks later a trace of sediment was noted and hence the material was redistilled through the apparatus shown on dr. A21-45-1 and physical constants redetermined. The 400-g. sample obtained was used in all of the tests recorded in this report. The data on this sample of CNCl before its delivery to the Medical Research Division are outlined below:

Date of delivery:	January 31, 1941.	
Appearance:	Water-white, mobile liquid.	
Quantity:	400 grams.	
Physical constants:		
	Found	Literature
Boiling point:	13.8°C.	12.55 to 13.0°C.
Melting point:	-7.05°C.**	-6.5 to -7.4°C.
Density, 0°C.	1.224	1.222
Chlorine content:	57.51%	Calculated, 57.68%

* The thermometer used for the boiling point and melting point was checked at the zero point.

** The sample which had a m.p. of -6.7°C. (see par. C, above) was considered to have higher purity.

VII. DISCUSSION.

The method of Jennings and Scott is marred by the formation of a volatile water-soluble dark-brown deposit which forms around the edge of the reaction mixture. The product probably owes at least part of its color to this substance. The zinc cyanide method is to be preferred because a cleaner product is obtained, and the reaction can be followed much more easily. When the chlorination is first begun, the soluble double salt is decomposed by the preferential chlorination of NaCN and the insoluble $Zn(CN)_2$ is precipitated, giving a milky suspension. After the exhaustion of the NaCN, the suspended $Zn(CN)_2$ is next chlorinated and the suspension begins to clear. Chlorination should be discontinued just short of completion, leaving some unreacted $Zn(CN)_2$. This ensures freedom from chlorine in the distilled product. The ratio of 4 moles of NaCN to 1 of $ZnSO_4$ is recommended. The NaCN and $ZnSO_4$ should be dissolved separately, each in one liter of water, and subsequently mixed with agitation. The reaction vessel should never be more than 3/5 full, since occasionally considerable foaming occurs, but usually this foaming stops during the course of the chlorination. Though the highest yield obtained in the present work was 73%, it is believed that a slightly higher one is possible. The values for the boiling point, melting point, and density agree well with those obtained in the most careful work reported in the literature (see table 2) and establish the purity of the sample obtained.

Much of the information relative to the stability of cyanogen chloride was from wartime reports, which are often vague and sketchy. It is seldom that the authors of these reports include any index of the degree of purity of the material under examination. In one instance where data are given (C.C.P. 47) in the studies of storage in steel, the CNCl is stated to have a freezing point of -8.3°C., which by comparison with other reported values (see table 2) would indicate that the material was not very pure. Hence the reliability of many of these wartime results must be questioned.

Table 2

Physical Constants.

Boiling point (°C.).	
12.66°/760 mm.	Regnault, Jahresber. 1863, 70.
12.5°/755 mm.	Mauguin and Simon, Ann. Chim. (9) 15, 41 (1921).
12.55°/760 mm.	Cook and Robinson, J. Chem. Soc. 1935, 1001-5.
13.0°/760 mm.	Klemenc and Wagner, Z. anorg. allgem. Chem. 235, 427-30 (1938).
Melting point (°C.).	
-7.4° (or -7.04°)	Regnault (both values are given in Regnault's original monograph according to the abstract in Jahresber. 1863, 74).
-7° to -6°	Mauguin and Simon.
-6.5° ± 0.2°	Klemenc and Wagner.
Density at 0°C.	
1.222	Mauguin and Simon.
1.222	Cook and Robinson.

The problem of stabilizing CNCl concerns itself with the polymerizing tendency, since hydrolysis can be prevented. CNCl is said to be stable in the presence of acetic anhydride, arsine, arsenic trichloride, chloroacetophenone, mustard or chloropicrin, but the information available is extremely meager. The effects of these substances merit reexamination. Indeed, it is believed that a fundamental study of the mechanism of the polymerization reaction might be a necessary preliminary to the selection of a suitable stabilizing agent. Furthermore, some additional light thrown on the more academic problem of the chemical constitution of CNCl might prove helpful.

In the light of the additional information contained in this report, in E.A.T.R. 360, Hydrocyanic Acid; Median Lethal Concentration for Mice, 2- and 30-Minute Exposures, and in E.A.T.R. 354, Phosgene; Median Lethal Concentration for Mice, 2- and 30-Minute Exposures, the indicated relative values of phosgene, cyanogen chloride, and hydrocyanic acid as quick-acting nonpersistent agents has again been studied. The following paragraphs discuss the characteristics outlined in project specification A 3 which are believed to be of paramount importance in the evaluation of such an agent.

Persistence.

All three of these compounds meet the requirement for nonpersistence.

Speed of Action.

In determining the median lethal concentration for hydrocyanic acid in all runs regardless of the concentration or time of exposure the mice were in a state of complete collapse when withdrawn from the gassing chamber. Practically all of the deaths occurred during the exposure to the agent.

With cyanogen chloride again all the mice were in a state of complete collapse when removed from the gassing chamber. For the 2- and 10-minute exposures those mice which revived, in almost all cases, survived the 10-day observation period. With a 30-minute exposure to a lower concentration there was a considerable number of delayed deaths.

In the tests on phosgene there was no collapse in the chamber and no immediate deaths were obtained.

These tests show the relative speed of action of these three compounds and indicate the failure of phosgene to meet this requirement.

Median Lethal Concentration.

The median lethal concentrations of these compounds are given in the following table. The references to the sources of these data will be found in part II, page 28. The median lethal concentration values are also given divided by the density of the respective compounds to show the relative volume ratios because shell are loaded to constant volume rather than constant weight.

Agent	Density	Exposure					
		2 min.		10 min.		30 min.	
		m.l.c.	m.l.c./d.	m.l.c.	m.l.c./d	m.l.c.	m.l.c./d.
	g./ml.	mg./l.	mg./l.	mg./l.	mg./l.	mg./l.	mg./l.
CG	1.4	2.3	1.64	0.375	0.268	0.112	0.08
CNCl	1.2	3.1	2.58	0.75	0.625	0.46	0.383
HCN	0.7	0.64	0.914	0.228	0.326	0.185	0.264

Phosgene has been included in this table for the sake of comparison although the lack of immediate deaths and collapse in determining the median lethal concentration at 2, 10, and 30 minutes indicates that it is not sufficiently rapid in producing deaths at these concentrations to be considered a quick-acting agent.

Both cyanogen chloride and hydrocyanic acid produced collapse during exposure and immediate deaths but considerably higher concentrations of cyanogen chloride were required. This is true when the comparison is made on either the weight or volume basis.

Procurability.

Hydrocyanic acid is produced on a commercial scale by a number of manufacturers, and procurement should offer no problem.

Phosgene is produced commercially to a limited extent but has been manufactured by the Chemical Warfare Service and plant designs are available.

Cyanogen chloride is not produced commercially and the Chemical Warfare Service has no plant designs for its manufacture.

Stability.

Means of stabilizing hydrocyanic acid have been investigated extensively by various industrial concerns, and these results have been made available to the Chemical Warfare Service. They indicate sufficient stability for this use but extended storage for more than one year is not recommended.

Phosgene appears to be sufficiently stable in storage for this use.

The stability of cyanogen chloride has received little study, consequently a very considerable amount of work would be necessary before its use could be recommended.

Warning Action.

Hydrocyanic acid has no very pronounced odor but is considered to be detectable by most people when breathed. Phosgene has a much more pronounced odor and is easily detectable. Cyanogen chloride is a powerful lacrimator, even in low concentrations. It is used as a warning agent in hydrocyanic acid fumigation.

Canister Penetration.

The protection afforded against these gases by the M1XA1 canister can be expressed as the number of grams of each which will be absorbed. This value will vary somewhat with the concentration of the gas, but the following values can be used for purposes of comparison:

Agent	Absorbed by M1XA1 canister
	g.
Phosgene	32
Hydrocyanic acid	6
Cyanogen chloride	3-4

Examination of these data show that the capacity of the canister for absorbing phosgene is so great that there is no threat of a break under any normal conditions in the field. Hydrocyanic acid and cyanogen chloride are much less readily absorbed and long-continued breathing of these gases could result in a break of the canister. Cyanogen chloride holds the advantage in this respect.

Summary.

Consideration of the above points concerning these agents indicates that phosgene does not meet the requirements for a quick-acting nonpersistent agent because immediate deaths or collapse were not produced.

Cyanogen chloride fails to meet these requirements in that too high a concentration is required, it is not procurable commercially and no plant designs are available; its stability has not been investigated and its powerful lacrimatory action serves as an effective warning of its presence.

Hydrocyanic acid is considered to most nearly meet the requirements for a quick-acting nonpersistent agent.

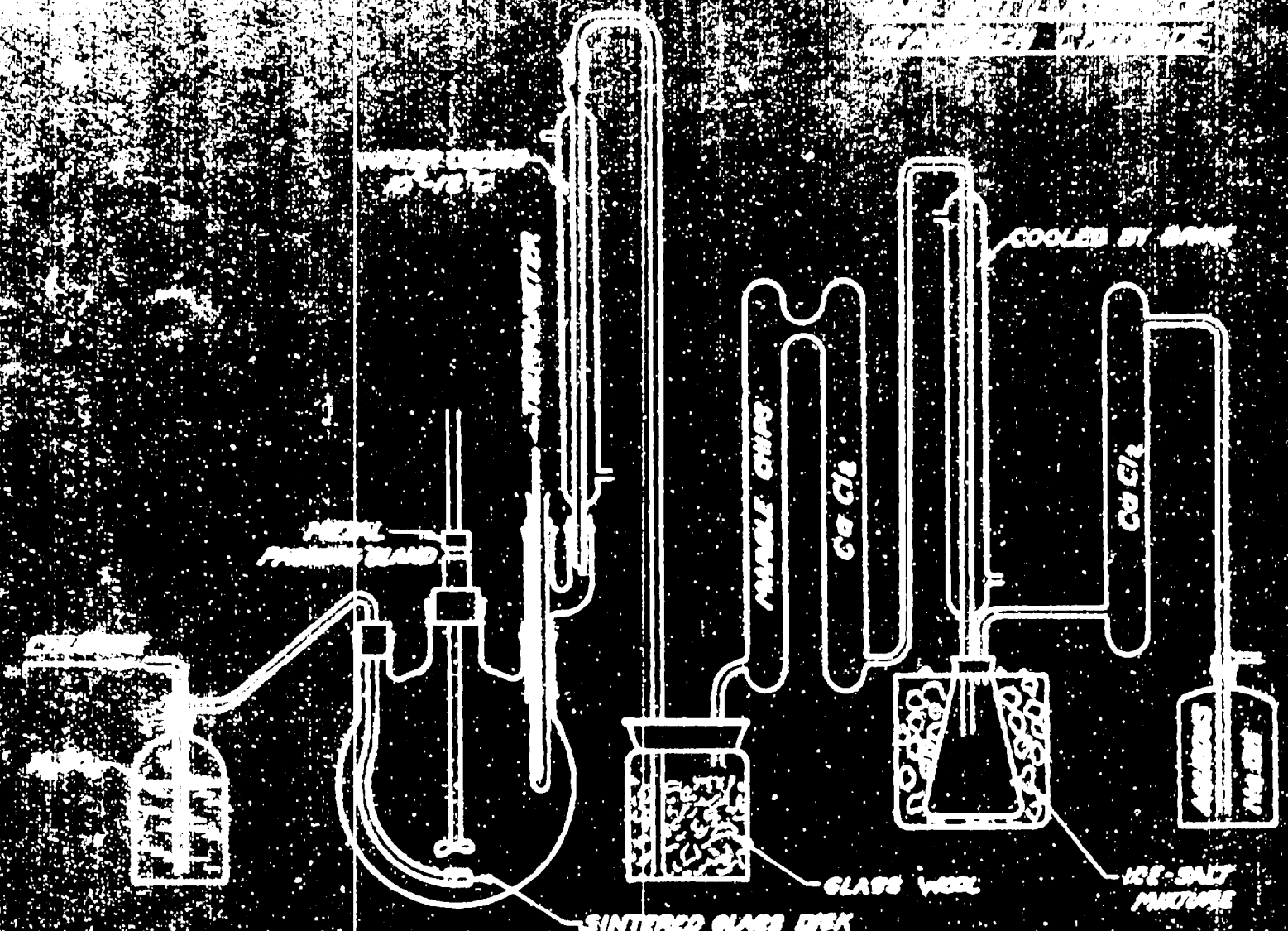
VIII. CONCLUSIONS.

1. Pure CNCl can be prepared by the $Zn(CN)_2$ method.

2. The data on the stability of CNCl are fragmentary and inconclusive. No fundamental studies on the mechanism of the polymerization reaction have ever been made.

3. Definite agreement as to the chemical constitution of CNCl has not been reached, but the most recent work favors the nitrile structure.

4. Cyanogen chloride does not meet the characteristics required for a nonpersistent agent to a sufficient extent to warrant further development for this use.


COOLED BY WATER
MANGANESE DIOXIDE
$CaCl_2$
$CaCl_2$
GLASS WOOL
ICE-SALT MIXTURE
SINTERED GLASS DISK

CYANOGEN CHLORIDE.

Part II. Toxicity: Median Lethal Concentration for Mice.

I. INTRODUCTION.

One of the objects of project A 3.3-1 is to "reinvestigate the toxicity of cyanogen chloride under the latest conditions for conducting animal experimentation and establish the minimum lethal concentration for 2 minutes, for 10 minutes, and for 30 minutes".

The object of the work described in part II of this report was to determine the median lethal concentrations of cyanogen chloride for white mice exposed for 2 min., 10 min., and 30 min. and observed for 10 days. Similar determinations have been made for phosgene and for hydrocyanic acid in order that the toxicity of the three compounds may be compared.*

II. HISTORICAL.

A great deal of work has been done on cyanogen chloride dating back to the first World War and before.

The toxicity of this compound has been determined for mice exposed for various periods of time. Early Chemical Warfare Service reports (P.R. 33, 41, and 59) indicate that the median lethal concentration of cyanogen chloride for mice, for a 10-min. exposure period, is between 0.2 and 0.5 mg./l. P.R. 222 reports experimental data for exposure period of 7-1/2 and 30 min., and 1, 2, 3, and 4 hr., and presents a chart showing a smoothed curve drawn from the plotted data (including the earlier data for 10-min. exposures). According to this curve, the "toxic concentration" (usually interpreted as that which killed from 50-70% of the animals exposed) for a 10-min. exposure is 0.64 mg./l. and for a 30-min. exposure, 0.38 mg./l. E.A.T.R. 120 establishes a median lethal concentration for 10 min. of 0.74 mg./l. for a 24-hr. observation period. The median lethal concentration for a 10-min. exposure and a 10-day observation period is 0.69 mg./l. according to calculations (E.A.T.R. 109, supplement 1) based on data submitted in E.A.T.R. 120.

*4th ind., CWS 400.112/137 secret, OG, EA, May 1, 1941, to C of CWS, on basic letter, same file, OG, EA, Mar. 6, 1941, subject, A 3.5-1, E.A.T.R. 340, HDN, Stability in Shell, Status Report, 1940, to C of CWS.

III. EXPERIMENTAL.

A. Material.

The cyanogen chloride used in all the runs was delivered to the Medical Research Division on January 31, 1941 by the Research Division, Edgewood Arsenal. It was described as follows:

Purity:	99.71% by Cl.
Boiling point:	13.8°C. at 760 mm.
Melting point:	-7.05°C.
Solubility:	soluble in alcohol and ether.
Stability:	stable towards atmospheric oxygen and moist air; probably not stable towards water.

The sample amounted to 400 g.

B. Animals.

The white mice used in these experiments were purchased from dealers. Three lots were used. Twenty five mice from each lot were set aside as controls and the normal daily death rate was determined from them. Pertinent data are tabulated below:

Mouse lot	Date received	Observation period	Normal daily death rate
		days	%
6	1/31/41	17	0.7
7	2/4/41	18	0.22
8	2/13/41	20	0.36

C. Apparatus.

The small gassing chamber (capacity 629 l.) and the apparatus used for setting up the various concentrations of cyanogen chloride in the chamber are shown in photograph 8168. Not in the photograph is the beaker used as an ice bath in which the bubbler was immersed during each run.

The apparatus used for collecting samples of the gas-air mixture for analysis is that shown in photograph 8422, except that only the large sampling tube was used.

D. Procedure.

The liquid cyanogen chloride was volatilized from a bubbler by passing nitrogen through it. The rate of vaporization was controlled by the rate of flow of the nitrogen, which was measured by a flowmeter in the line, and regulated by a controlled leak between the flowmeter and the bubbler, and a needle valve. The agent was kept at 0°C. by immersion in an ice bath. The resulting cyanogen chloride-nitrogen mixture was introduced into a glass mixing bowl, through which the affluent air to the chamber passed, carrying the agent into the chamber. The airflow through the chamber was 250 l./min. as measured by an orifice meter in the effluent air line.

The mice were placed in a wire cage having 20 compartments and fitted with a sliding wire cover. The cage was instantaneously introduced into, or withdrawn from the gassing chamber by means of a gas-tight cradle.

Concentrations were established in the gassing chamber by the following method. The airflow through the chamber was started and set at 250 l./min. The bubbler was weighed carefully. To prevent loss while weighing, the cyanogen chloride in the bubbler was frozen solid for that operation by dipping for a short time into a mixture of 100 parts of calcium chloride hexahydrate and 70 parts of snow contained in a Dewar flask. The bubbler was then connected to the rest of the apparatus in the proper manner (see photograph 8168), the nitrogen control leak being left open. The flow of nitrogen was started and maintained at an arbitrarily chosen flowmeter level by means of the needle valve. The bubbler stopcock was then opened and the control leak closed quickly by a pinchclamp, forcing the nitrogen through the bubbler. At the same time a stopwatch was started.

According to the equation $t_{99} = 4.6 \frac{\text{chamber vol.}}{\text{airflow}}$ a 629-l. chamber having an airflow of 250 l./min. requires 12 min. to reach 99% theoretical concentration. The gas-air mixture was therefore allowed to pass through the chamber for 15 min. in order to establish a constant concentration therein. At the 15th minute the

mice were introduced into the chamber. Twenty mice were used in each run; the exposure period was 10 min. and the observation period was 10 days.

Nominal concentrations were calculated from the loss in weight of the bubbler, the rate of airflow through the chamber, and the time during which vaporization from the bubbler took place, as follows:

$$\text{Nominal concn. (mg./l.)} = \frac{\text{Loss in weight of bubbler (mg.)}}{\text{Airflow thru chamber (l./min.)} \times \text{time (min.)}}.$$

Sampling of the gas-air mixture in the chamber was started simultaneously with the introduction of the mice into the chamber.

E. Analysis.

The gas-air samples withdrawn from the gassing chamber were analyzed for cyanogen chloride by absorbing it in 25 ml. of a solution containing 70% of 95% ethyl alcohol and 30% of 2N sodium hydroxide. This was then neutralized with nitric acid and a slight excess of the latter was added. Total chlorides were found by the Volhard method.

$$\text{Anal. concn. (mg./l.)} = \frac{(\text{ml.}AgNO_3 \times \text{N.F.}^* - \text{ml.KSCN} \times \text{N.F.})}{\text{True volume of sample (l.)}} \times 61.5$$

The true volume was found by the following:

$$\text{True volume} = \frac{\text{Barometer reading} - \text{meter manometer}}{\text{Barometer reading}} \times \text{volume}$$

The size of the sample as read from the meter was 10 l. in the runs for 2- and 10-minute exposures and 25 l. in the runs for 30-minute exposures.

F. Results.

The results for the three different exposure periods are shown in tables 1, 2, and 3.

---

* Normality factor.

Table 1.

Toxicity of Cyanogen Chloride to Mice: 2-min. Exposure.

Run	Date	Concn. Nom.	Concn. Anal.	Mice used	Temp.	Rel. hum.	Daily deaths Imm.*	1	2	3	4	5	6	7	8	9	10	10
	1941	mg./l.	mg./l.		°C.	%												%
1	2/10	1.37	1.30	Lot 7	22	20	0	0	0	0	0	0	0	0	0	0	0	0
2	2/10	1.52	1.43	Lot 7	22	20	0	0	0	0	0	0	0	0	0	0	0	0
3	2/10	1.67	1.51	Lot 7	23	20	2	2	2	2	2	2	2	2	2	2	2	10
4	2/10	2.40	1.83	Lot 7	25	18	2	2	2	2	4	4	4	4	4	4	4	20
5	2/10	2.68	2.36	Lot 7	25	18	0	0	0	0	0	0	0	0	0	0	0	0
8	2/11	3.11	2.81	Lot 7	19	30	11	11	11	11	12	12	12	12	12	12	12	60
9	2/11	3.21	3.03	Lot 7	19	30	15	15	15	15	15	15	15	15	15	15	15	75
6	2/10	3.88	3.24	Lot 7	25	18	13	13	13	13	13	13	13	13	13	13	13	65
7	2/10	4.42	3.56	Lot 7	25	18	20	20	20	20	20	20	20	20	20	20	20	100

*Deaths occurring during exposure, or within 1 hr. thereafter, are classed as immediate.

Table 2.

Toxicity of Cyanogen Chloride to Mice: 10-min. Exposure.

Run	Date	Concn. Nom.	Concn. Anal.	Mice used	Temp.	Rel. hum.	Imm.*	Daily deaths 1	2	3	4	5	6	7	8	9	10	10
	1941	mg./l.	mg./l.		°C.	%												%
1	2/4	0.34	0.35	Lot 6	19	30	0	0	0	0	0	0	0	0	0	0	0	0
2	2/4	0.51	0.45	Lot 6	19	30	0	0	0	0	0	0	0	0	0	0	0	0
6	2/4	0.59	0.50	Lot 6	23	30	3	3	3	3	3	3	3	3	3	3	3	15
3	2/4	0.67	0.65	Lot 6	19	30	1	1	1	1	1	1	1	1	1	1	1	5
7	2/5	0.67	0.58	Lot 6	22	29	4	4	4	4	4	4	4	4	4	4	4	20
5	2/4	0.73	0.58	Lot 6	22	30	9	9	9	9	9	9	9	9	9	9	9	45
8	2/5	0.85	0.80	Lot 6	22	29	17	17	17	17	17	17	17	17	17	17	17	85
4	2/4	0.87	0.82	Lot 6	21	32	18	18	18	18	19	19	19	19	19	19	19	95

*Deaths occurring during exposure, or within 1 hr. thereafter, are classed as immediate.

Table 3.

Toxicity of Cyanogen Chloride to Mice: 30-min. Exposure.

Run	Date	Concn. Nom.	Concn. Anal.	Mice used	Temp.	Rel. hum.	Daily deaths Imm.*	1	2	3	4	5	6	7	8	9	10	10
	1941	mg./l.	mg./l.		°C.	%												%
1	2/12	0.08	0.09	Lot 7	21	37	0	0	0	0	0	0	0	0	0	0	0	0
2	2/12	0.18	0.18	Lot 7	23	30	0	0	0	0	0	0	0	0	0	0	0	0
3	2/13	0.36	0.34	Lot 8	27	30	0	1	1	1	1	1	1	1	1	1	1	5
4	2/14	0.39	0.33	Lot 8	22	24	4	5	8	8	8	8	8	8	8	8	8	40
5	2/14	0.46	0.40	Lot 8	22	24	4	7	10	12	12	12	12	12	12	12	13	65
6	2/14	0.50	0.41	Lot 8	21	24	5	6	6	6	6	6	6	6	6	6	6	30
7	2/14	0.56	0.48	Lot 8	20	24	19	19	19	19	19	19	19	19	19	19	19	95

*Deaths occurring during exposure ,or within 1 hr. thereafter, are classed as immediate.

The results shown in the above tables are plotted in charts 1, 2, and 3 by the use of probits (as done in E.A.T.R. 109, Suppl. 1). This method of straightening the usual S curve is explained in that reference. Nominal concentrations were used for the plots. The median lethal concentrations, as read from the charts, are as follows:

Exposure	Observation	M.L.C.	Average deviation (a.d.)
		mg./l.	
2 min.	10 days	3.1	± 0.280
10 min.	10 days	0.75	± 0.027
30 min.	10 days	0.46	± 0.03

The average deviation (a.d.) is used as a measure of the internal consistencies of charts 1, 2, and 3.

The mice displayed practically the same symptoms in all runs at all exposures. These were, in order, eye irritation, excitement, irritation of the upper respiratory passages, gasping, occasional convulsions, collapse, and in some cases death. With the mice exposed for 2 and 10 minutes the great majority of the deaths occurred during exposure. Only in three of the seventeen runs were there any delayed deaths. However with the mice exposed for 30 min. there was a considerable number of delayed deaths. Four of the five runs showing deaths exhibited this phenomenon.

IV. DISCUSSION.

A. Concentration Data.

The relation between the nominal concentrations and the analytical concentrations is shown in table 4. This is compiled in order of increasing nominal concentrations.

Table 4.

Concentration Comparisons.

Concentration		Anal.
Nominal	Analytical	nom.
mg./l.	mg./l.	
0.082	0.087	1.06
0.179	0.179	1.00
0.344	0.349	1.01
0.364	0.335	0.92
0.393	0.325	0.83
0.464	0.397	0.86
0.496	0.406	0.82
0.508	0.447	0.88
0.556	0.484	0.87
0.585	0.500	0.86
0.671	0.645	0.96
0.674	0.575	0.85
0.732	0.584	0.80
0.845	0.797	0.94
0.874	0.820	0.94
1.366	1.295	0.95
1.523	1.430	0.94
1.674	1.509	0.90
2.398	1.825	0.76
2.676	2.360	0.88
3.111	2.810	0.90
3.205	3.030	0.95
3.875	3.240	0.84
4.415	3.560	0.81
	Average	0.897

B. Known Sources of Error in M.L.C.

Possible errors involved are tabulated below:

Source of error	Possible error %
1. Compound	
Purity, 99.71% by Cl	0.29
2. Mice	
10-day death rate: lot 6, 7.0%	Indeterminable
lot 7, 2.2%	"
lot 8, 3.3%	"
Exposure time, 10 min. ± 0.033 min.	0.33
Variation in age, sex, nutritional history, etc.	Indeterminable

Source of error	Possible error
3. Plot	
Accuracy: 1/20 in. = 0.05 mg./l. in chart 1	1.6
0.01 " " " 2 and 3	1.3-2.2
ca. 1% deaths between 25 and 75%	ca. 1
4. Analytical concentration, $C_a = m/v$	
m = total milligrams found by titration.	
ml. titrating solution near m.l.c. for,	
2-min. exposure 22 ± 0.05 ml.	0.13
10-min. exposure 5 ± 0.05 ml.	1.0
30-min. exposure 8 ± 0.05 ml.	0.63
v = volume of sample.	
near m.l.c. volume accuracy for,	
2-min. exposure 10 ± 0.01 l.	0.1
10-min. exposure 10 ± 0.01 l.	0.1
30-min. exposure 25 ± 0.01 l.	0.04
5. Nominal concentration, $C_n = R/Q$	
R = weight-loss/time.	
near m.l.c., weight loss was for,	
2-min. exposure 16 ± 0.001 g.	0.0063
10-min. exposure 5 ± 0.001 g.	0.020
30-min. exposure 5 ± 0.001 g.	0.020
time measured for,	
2-min. exposure 20.5 ± 0.033 min.	0.16
10-min. exposure 25 ± 0.033 min.	0.13
30-min. exposure 45 ± 0.033 min.	0.07
Q = airflow through chamber	4
Total possible known nominal and analytical errors* including purity.	
2-min. exposure	4.7
10-min. exposure	5.5
30-min. exposure	5.1

*Obtained by adding pertinent data in items 1, 4, and 5.

The average of 24 runs show that C_a differs from C_n by 10.3%, leaving an approximate unknown error of 5%.

C. Median Lethal Concentration for Mice.

The nominal concentrations were used to determine the median lethal concentrations of cyanogen chloride.

Cyanogen chloride in the higher concentrations and shorter exposures is of the "all or none" type. Those animals surviving the exposure period in the 2- and 10-min. exposures had excellent chances of reviving and were apparently unaffected within 24 hr. after gassing. The delayed death phenomenon occurred only in the 30-min. exposures. It was characteristic in the lower concentrations, where deaths were recorded for as many as 4 days after gassing. This is typical of long exposures at low concentrations of many toxics.

The action of cyanogen chloride upon the mice was very fast. Eye irritation usually was evident in between 30 to 60 seconds while the first excitement lasted only about 2 to 5 min., ending in complete collapse. In all runs, regardless of concentration or exposure time, the mice were in a state of complete collapse when withdrawn from the gassing chamber. However, recovery was equally quick. Those mice not dead on withdrawal, although in appearance without life, within 2 min. were moving about and were apparently completely recovered within 20 minutes after gassing. Even those which subsequently died in the 30-min. exposure runs presented this picture, leading to the opinion that the delayed deaths were therefore due to secondary phenomena such as pneumonia, or infection due to lowered resistance.

A comparison of this work with that previously done is shown in table 5.

Table 5.

Median Lethal Concentrations of Cyanogen Chloride for Mice; Comparative Data.

Exposure	New work	Previous investigations		Remarks
	Concn.	Concn.	Reference	
min.	mg./l.	mg./l.		
2	3.1	-	-	-
10	0.75	0.65	PR 222	From curve interpolation.
		0.69	EATR 109 Suppl.	Calculated from EATR 120.
30	0.46	0.5	CWM Vol. LVI	
		0.38	PR 222	From curve interpolation.

It is interesting to note that if the analytical concentrations are used to plot the m.l.c., it is lowered by 10%. This would make the m.l.c. for 10-min. exposures 0.675 mg./l. and for 30-min. exposures 0.41 mg./l., thus corroborating the previous work very closely. This is to be expected since only the analytical concentrations were used in the older determinations.

As per project A 3.3-1, a comparison of the lethality of phosgene, cyanogen chloride, and hydrocyanic acid is included herewith. The median lethal concentrations to mice for 2-, 10-, and 30-min. exposure periods and 10-day observation periods of the three above-mentioned compounds are as follows:

Compound	m.l.c. for 2-min. exp.	m.l.c. for 10-min. exp.	m.l.c. for 30-min. exp.
	mg./l.	mg./l.	mg./l.
Phosgene	2.35 (1)	0.375 (2)	0.112 (1)
Cyanogen chloride	3.1 (3)	0.75 (3)	0.46 (3)
Hydrocyanic acid	0.64 (4)	0.228 (5)	0.185 (4)

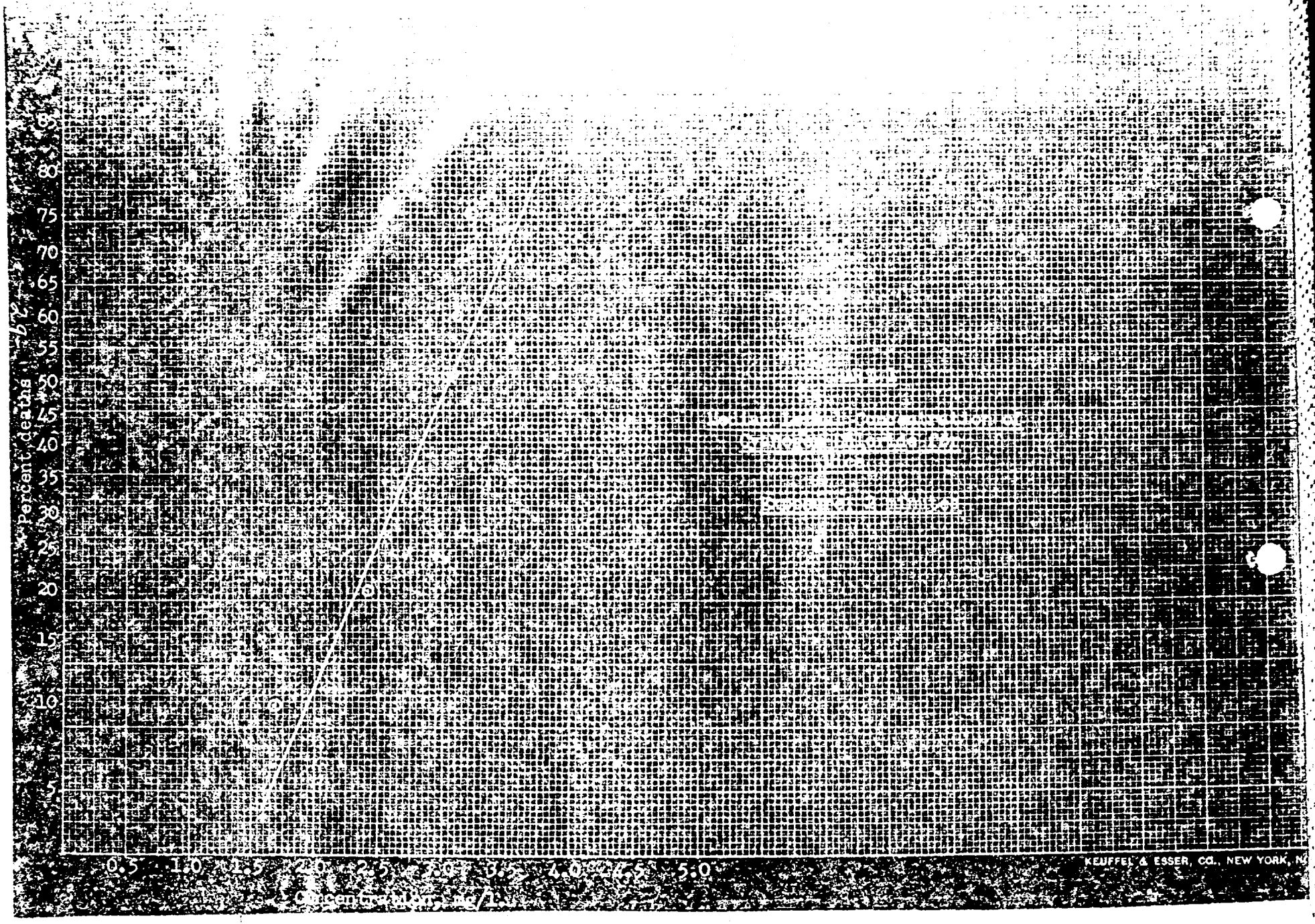
(1) E.A.T.R. 354. (2) E.A.T.R. 119. (3) This report.
(4) E.A.T.R. 360. (5) E.A.T.R. 136.

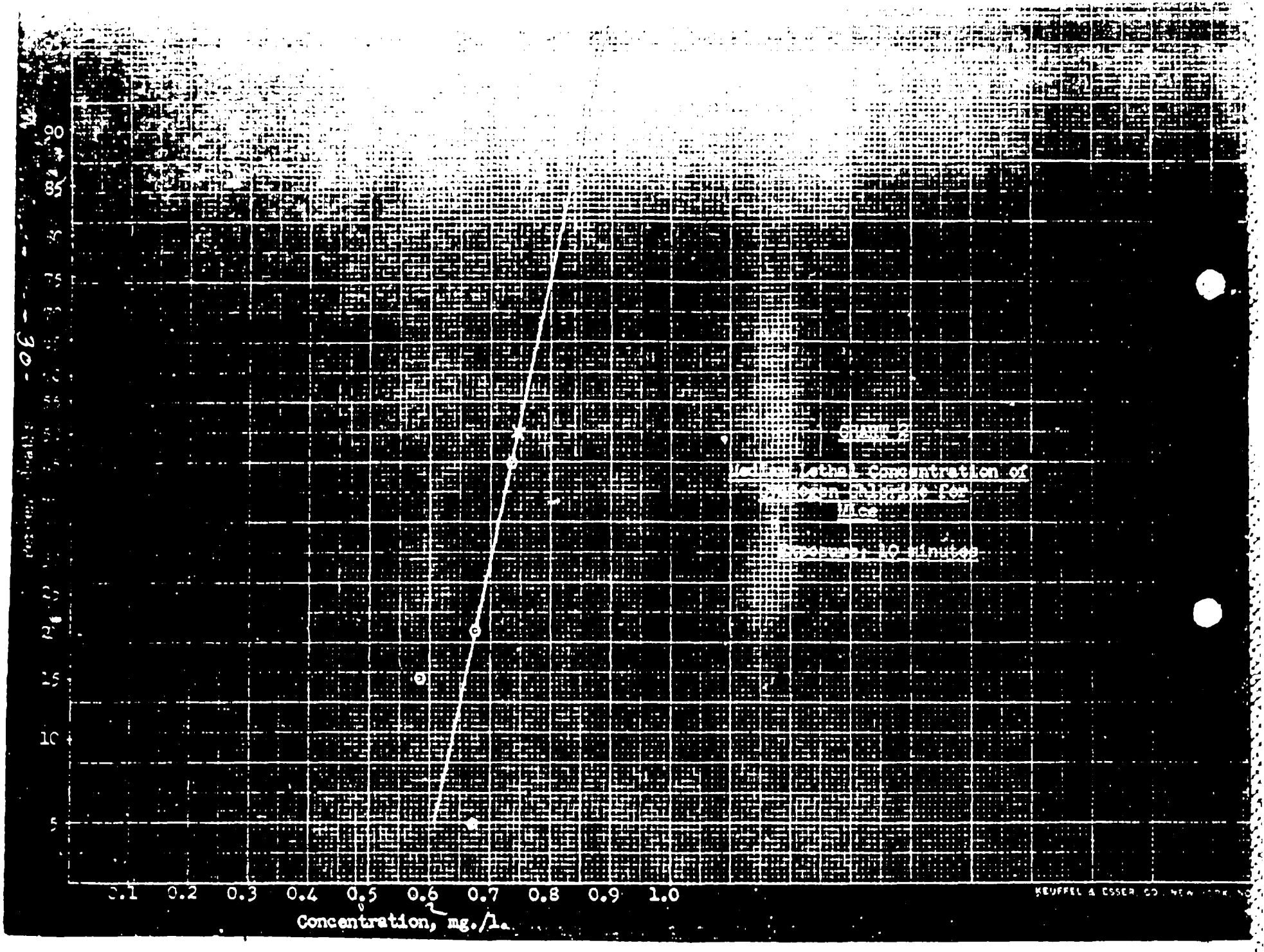
V. CONCLUSIONS.

1. The median lethal concentration of cyanogen chloride for mice, for an exposure period of 2 min. and an observation period of 10 days, is 3.1 mg./l., with an average deviation (for 5 runs) of 0.23 mg./l.

2. The median lethal concentration of cyanogen chloride for mice, for an exposure period of 10 min. and an observation period of 10 days, is 0.75 mg./l., with an average deviation (for 6 runs) of 0.027 mg./l.

3. The median lethal concentration of cyanogen chloride for mice, for an exposure period of 30 min. and an observation period of 10 days, is 0.046 mg./l., with an average deviation (for 5 runs) of 0.030 mg./l.

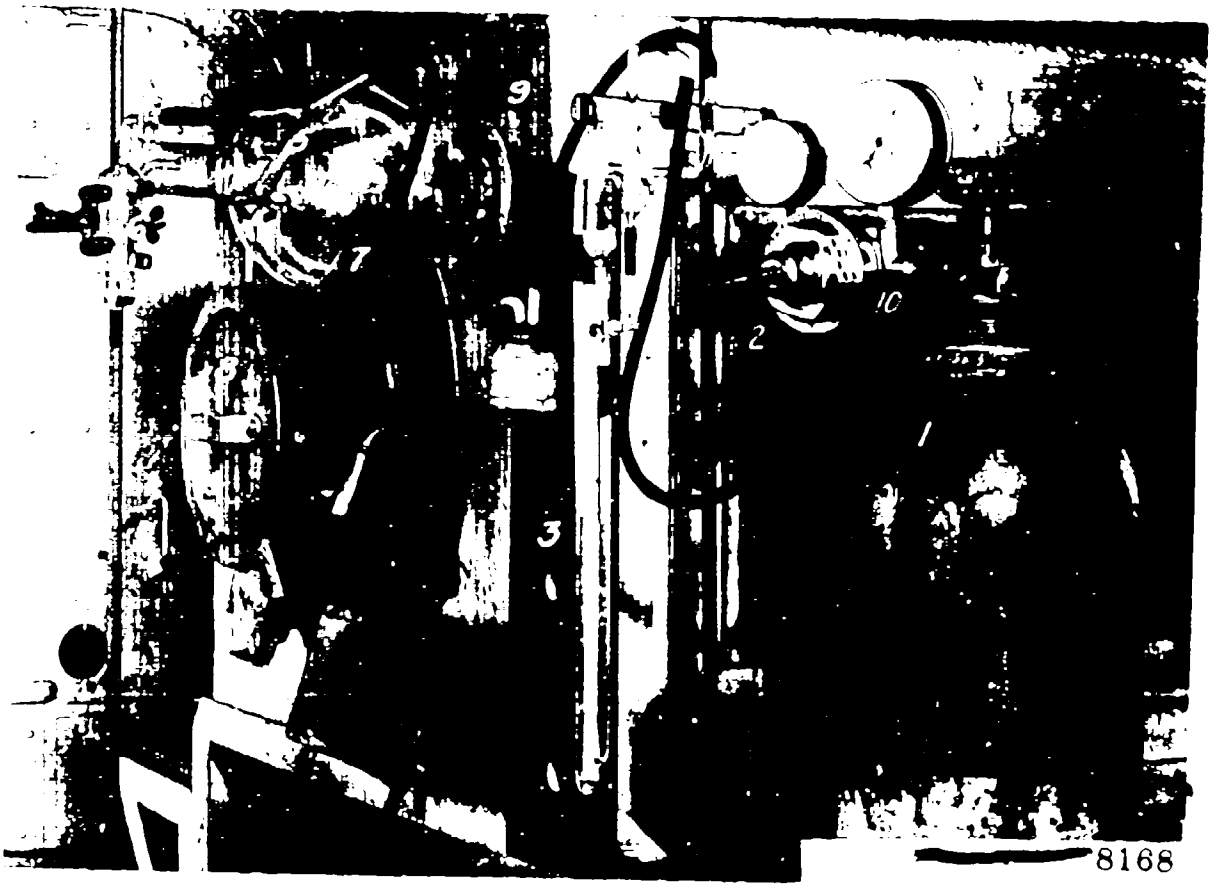

Percent deaths
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
Oxygen tension, mm/Hg
KEUFFEL & ESSER CO., NEW YORK, N



GRAPH 2

Median Lethal Concentration of Chlorine Dioxide for Mice

Exposure: 10 minutes



[illegible]

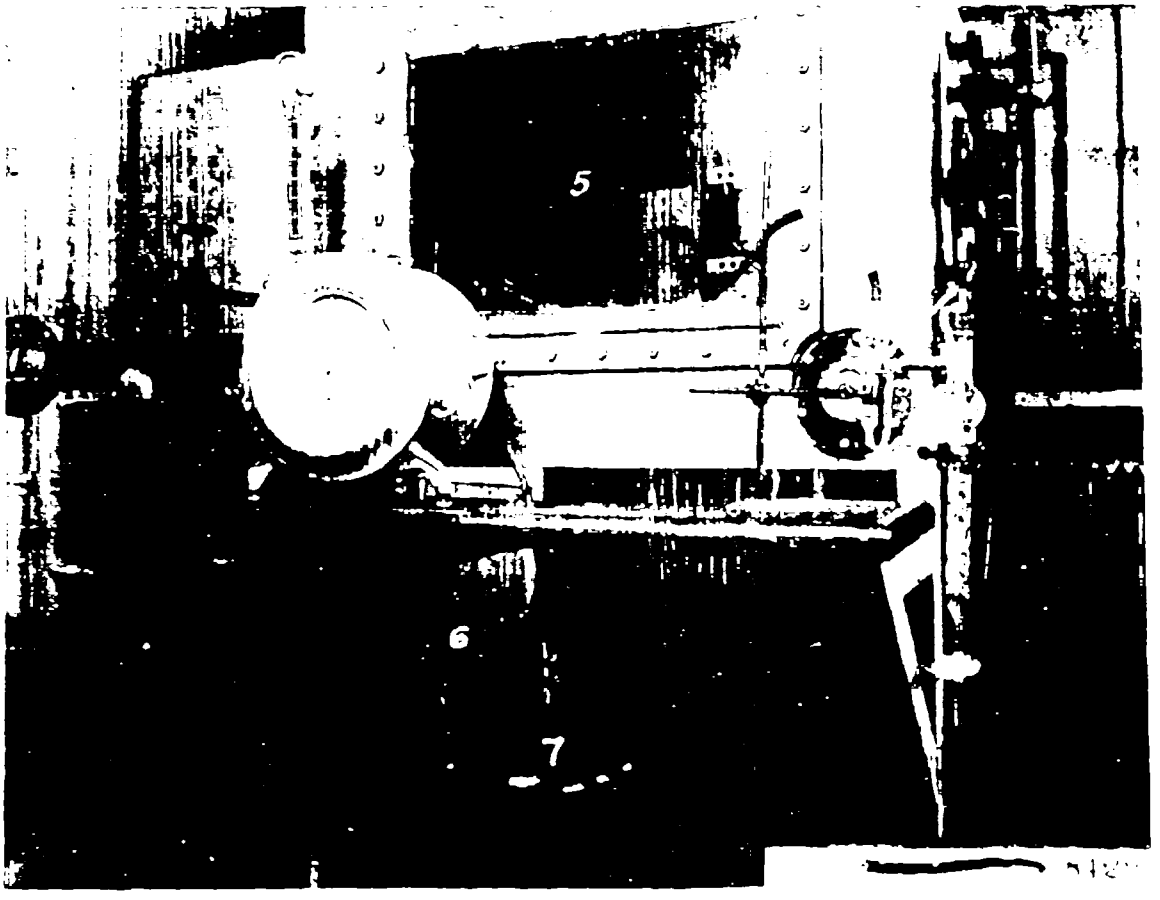
[illegible]:

[illegible]:

1. [illegible]
2. [illegible] valve.
3. Flow [illegible] of nitrogen.
4. Trap to [illegible] flowmeter [illegible].
5. Nitrogen [illegible].
6. Bubbler containing [illegible] chloride.
7. Lining bowl.
8. Instantaneous-exposure cradle.
9. [illegible]
10. [illegible]

[illegible]: [illegible]

[illegible]: Photograph [illegible] August [illegible], 1949.


5
6
7

Submitted:

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Research Division.

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Part II. S. D. Silver,*
Medical Research Div.

F. P. McGrath,*
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*Authors.

Part I.
Experimental work:
Started: Sept. 3, 1940.
Completed: Oct. 18, 1940.
Notebook 662.

Part II.
Experimental work:
Started: Feb. 3, 1941.
Completed: Feb. 26, 1941.
Notebooks 683, 726.

CYANOGEN CHLORIDE.
Part I. Preparation.
Part II. Toxicity: Median Lethal Concentration for Mice.

E.A.T.R. 341.

Project: A 3.3-1.

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REPLY TO
ATTENTION OF

27 AUG 14

AUG 2 7 2014

RDCB-DPS-RS

MEMORANDUM THRU Director, Edgewood Chemical Biological Center, (RDCB-D/Mr. Joseph Wienand), 5183 Blackhawk Road, Aberdeen Proving Ground, Maryland 21010-5424

FOR Defense Technical Information Center, 8725 John J. Kingman Road, Ft Belvoir, VA 22060

SUBJECT: Internal Request for Change in Distribution

1. This action is in response to an Edgewood Chemical Biological Center (ECBC) Internal Request for a Change in Distribution on documents related to cyanogen chloride.

2. The listed documents in the attachment have been reviewed by ECBC Subject Matter Experts and deemed suitable for the change in distribution to read "Approved for Public Release; distribution unlimited."

3. The point of contact is Adana L. Eilo, ECBC Security Specialist, (410) 436-2063, adana.l.eilo.civ@mail.mil.

Encl

MATTHEW A. SPAULDING
Security Manager

Printed on Recycled Paper

Cyanogen Chloride References

[1] Marshall, E.K. and Miller, E.J., *Toxicity of Cyanogen Chloride for The Dog, Rabbit, Guinea Pig, Rat and Mouse on Inhalation,* **Report No. 222** in Marshall, EK ed., **Pharmacological and Research Section Monographs**. War Department Chemical Warfare Service, Research Division, American University Experiment Station, Washington, DC, c. 1918. On file with the Historical Research and Response Team, Research, Development and Engineering Command, Aberdeen Proving Ground, MD. Unclassified, Dist. E, DoD Only.

[2] Miller, E.J. and Gross, J., *Report on G-178 (Cyanogen Chloride),* **CB-183864,** in Marshall, EK ed., **Pharmacological and Research Section Monographs**. War Department Chemical Warfare Service, Research Division, American University Experiment Station, Washington, DC, 18 April 1918. Unclassified, Dist. E, DoD Only.

[3] *Monthly Progress Report,* **CB-186024,** Chemical Corps, Army Chemical Center, MD, 15 June 1944, Unclassified, Dist. E, DoD Only.

[4] McGrath, F.P., Sober, H.A., and Silver, S.D., *Cyanogen Chloride LC 50 for Goats: 2 Min. Exposure,* **CB-015759**, Chemical Corps Technical Command, Army Chemical Center, MD, 28 March 1944, Unclassified, Dist. D, DoD/Contractors Only.

[5] Silver, S.D. and McGrath, F.P., *Cyanogen Chloride, Part 1. Preparation. Part 2. Toxicity: Median Lethal Concentration for Mice,* **EA-TR-341**, Edgewood Arsenal, Aberdeen Proving Ground, MD, 30 January 1942, Unclassified, Dist. D, DoD/Contractors Only.